Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

VOL. 52 JANUARY 1959 NO. 1

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Fifty-Third Annual Meeting, November 16-19, 1959, Atlanta, Georgia

JANUARY 1959

VOLUME 52 NUMBER 1

Southern Medical Journal

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

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Published monthly by the Southern Medical Association, 2601 Highland Avenue, Birmingham 5, Alabama. Annual subscription, $10.00. Single copies, $1.00 each. **Copyright, Southern Medical Association, 1959.**

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

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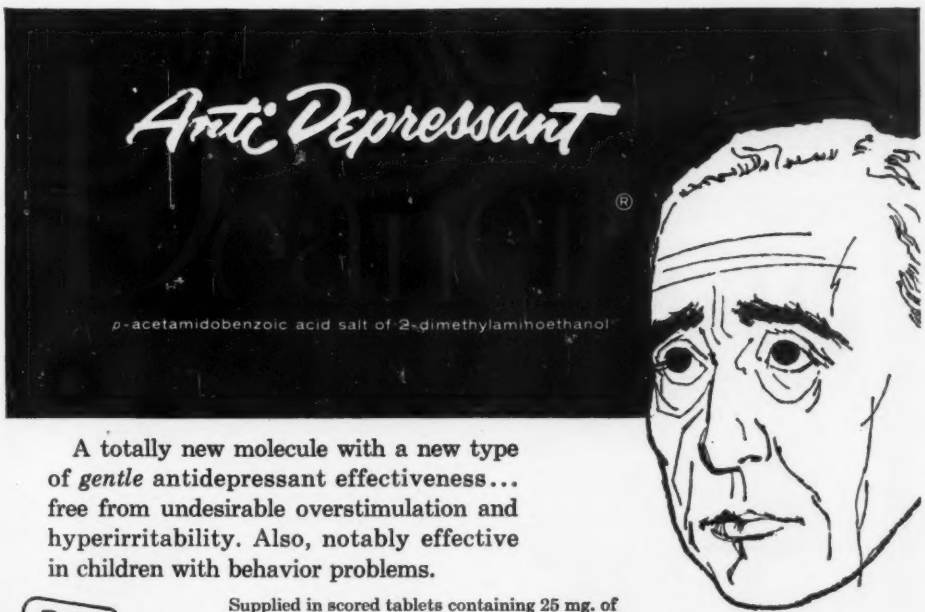
- with chronic fatigue
- with neurasthenia
- with difficulty in concentrating



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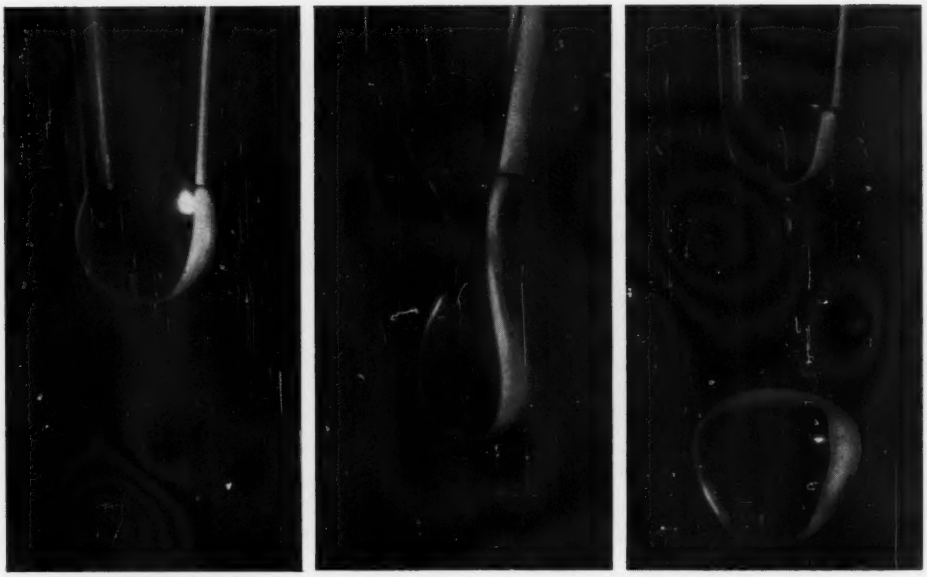

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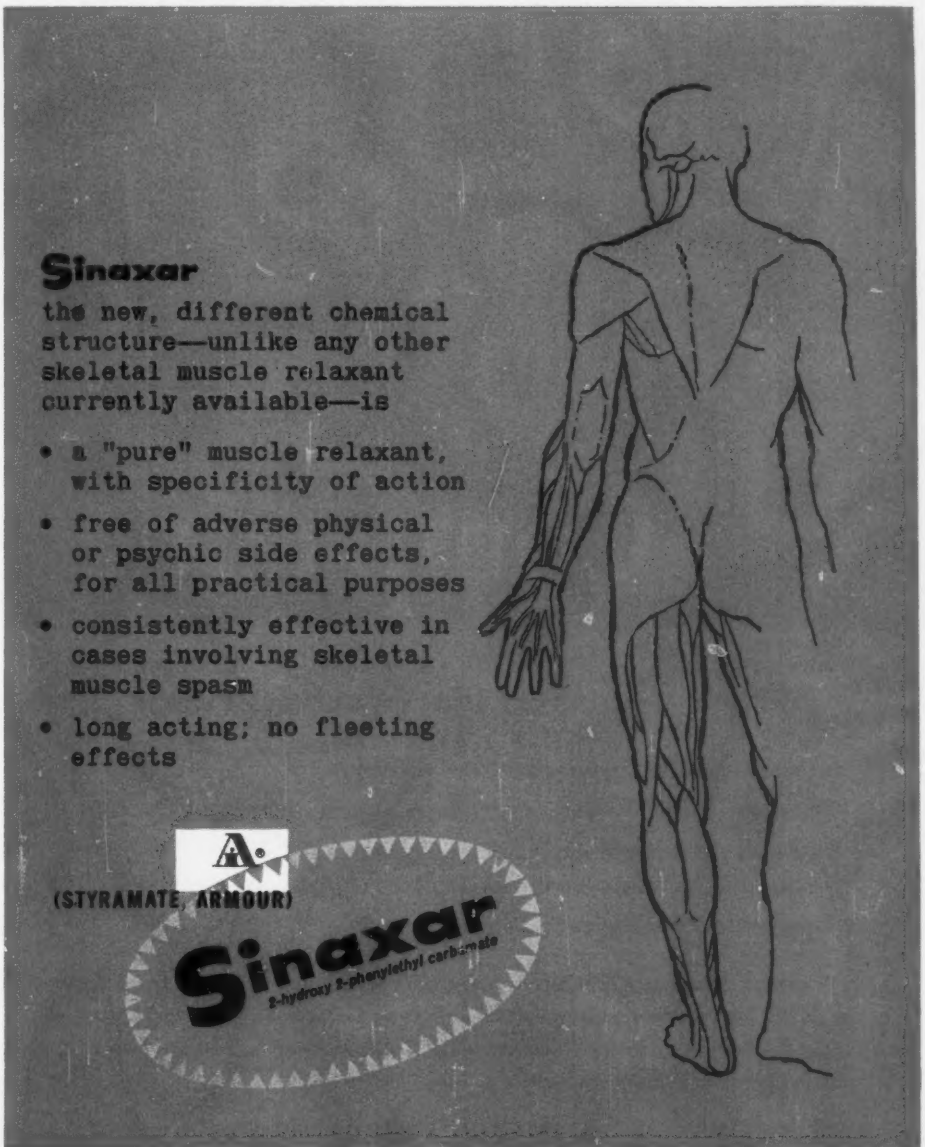
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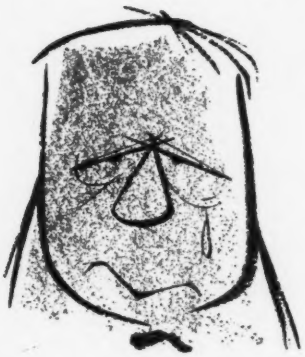

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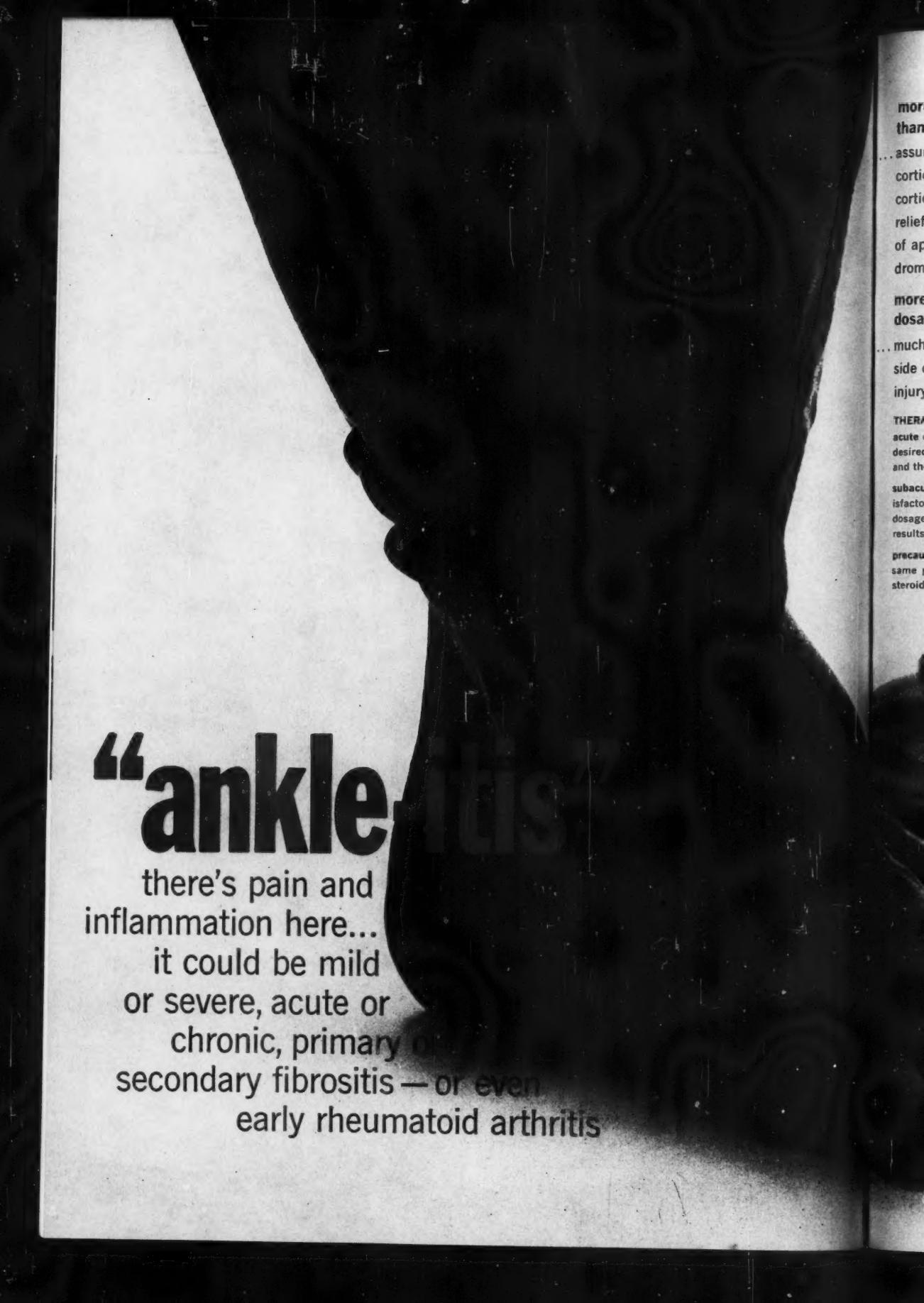
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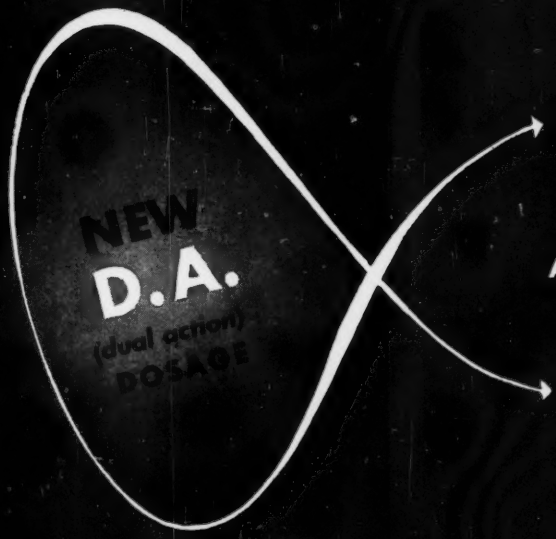

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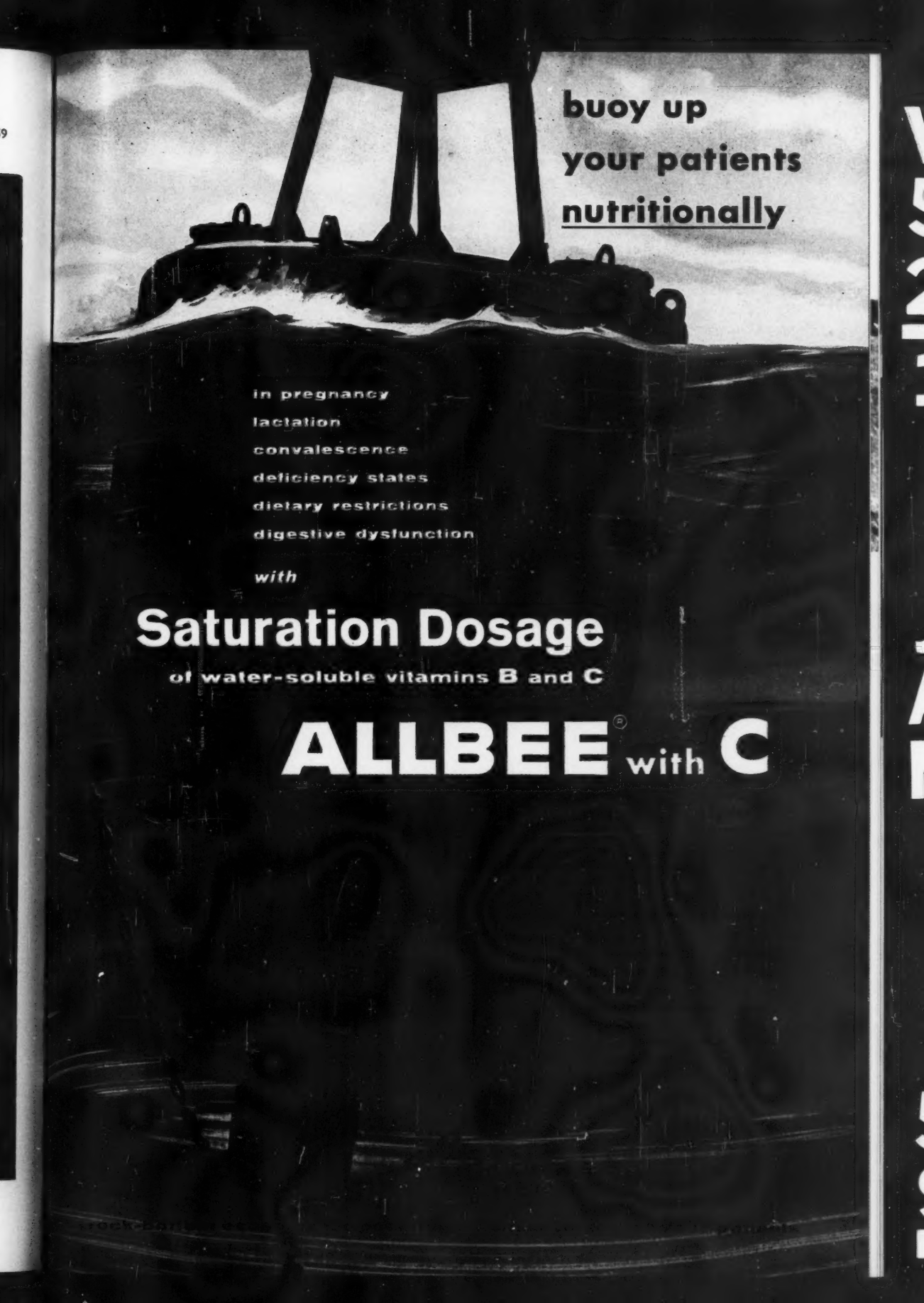
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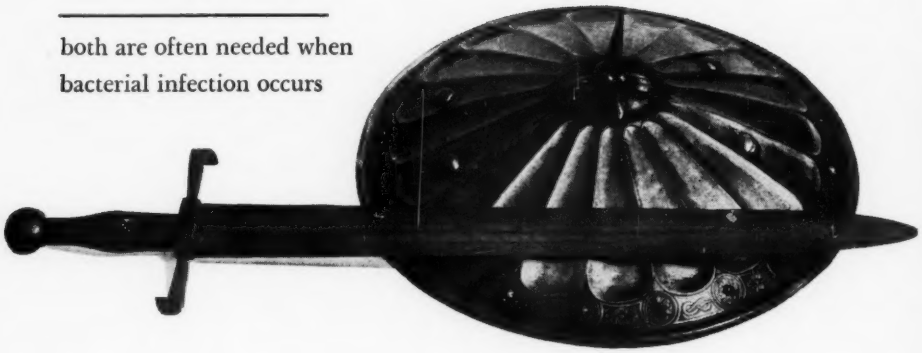

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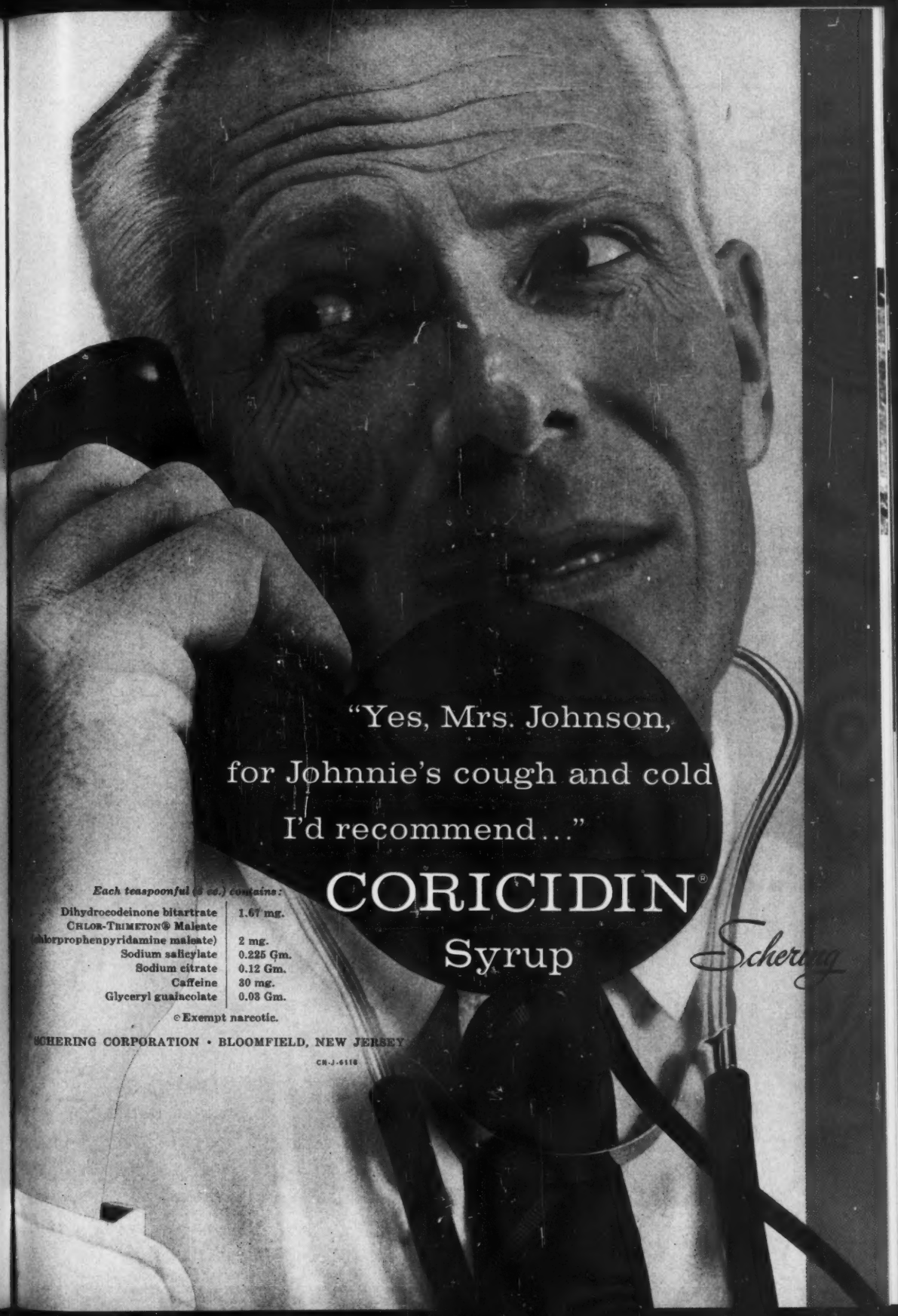
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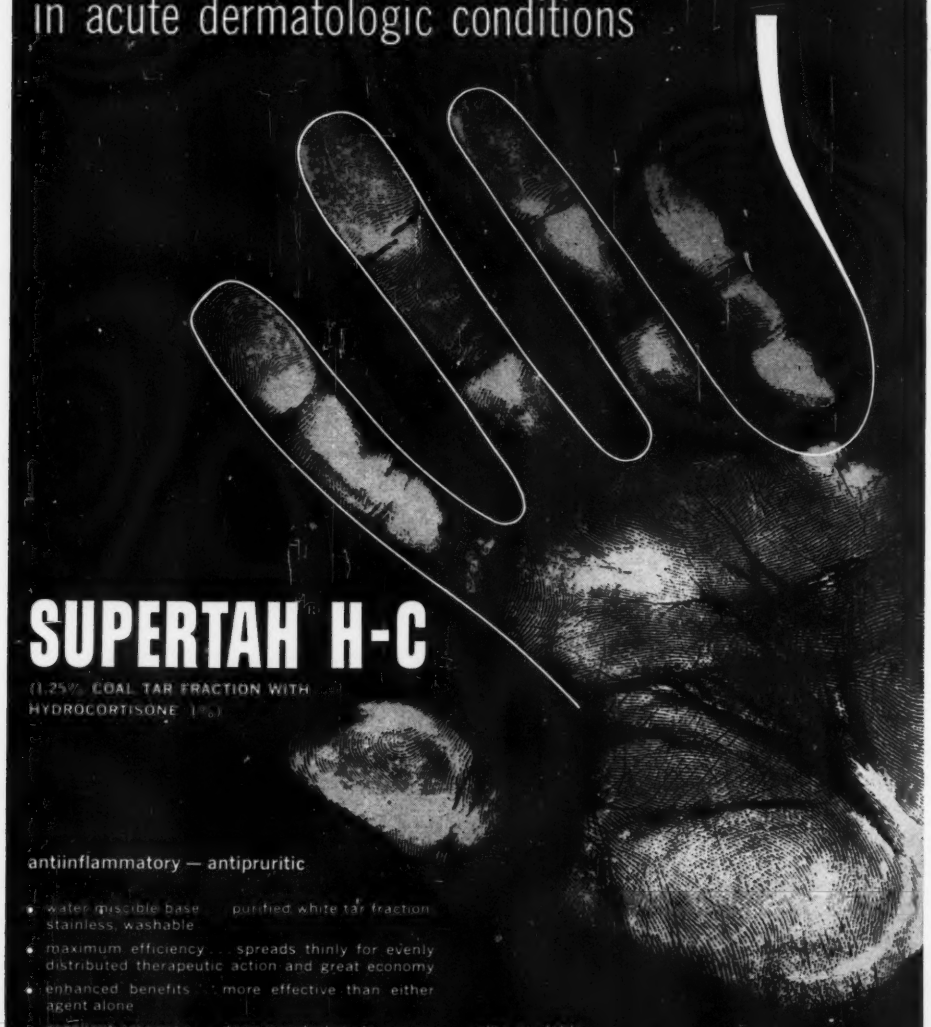

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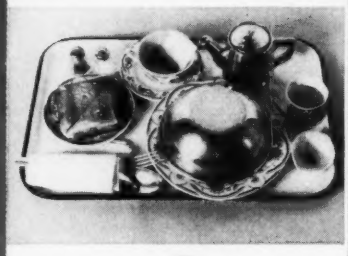

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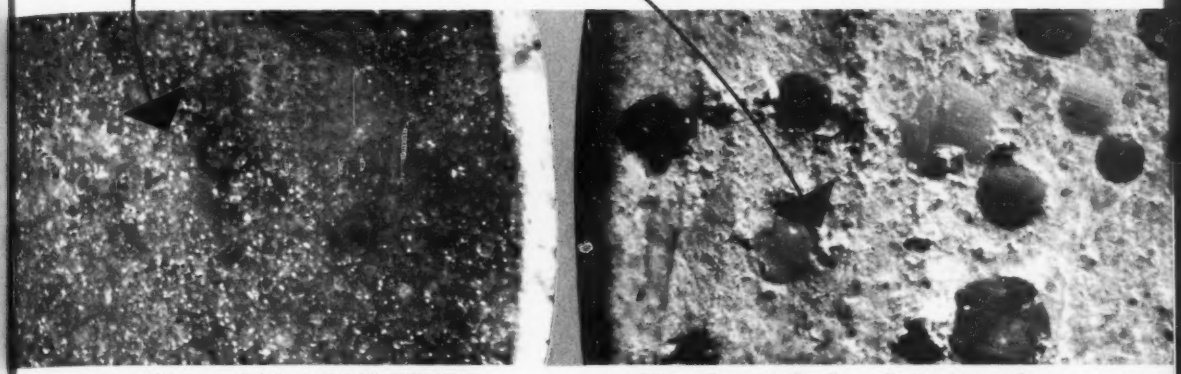

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1. Lewis, J.M., et al.: J. Pediatrics, *31*:496

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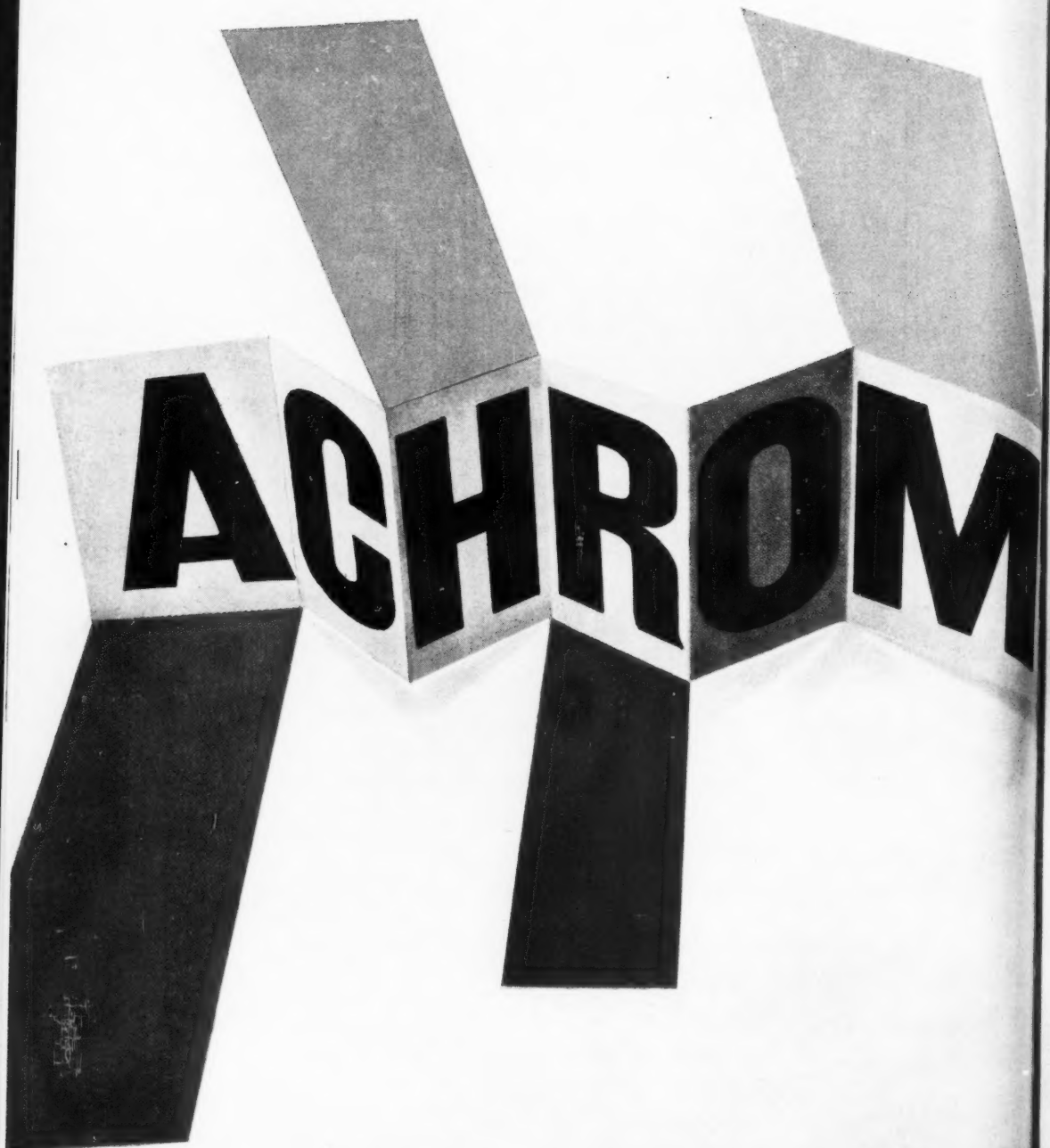
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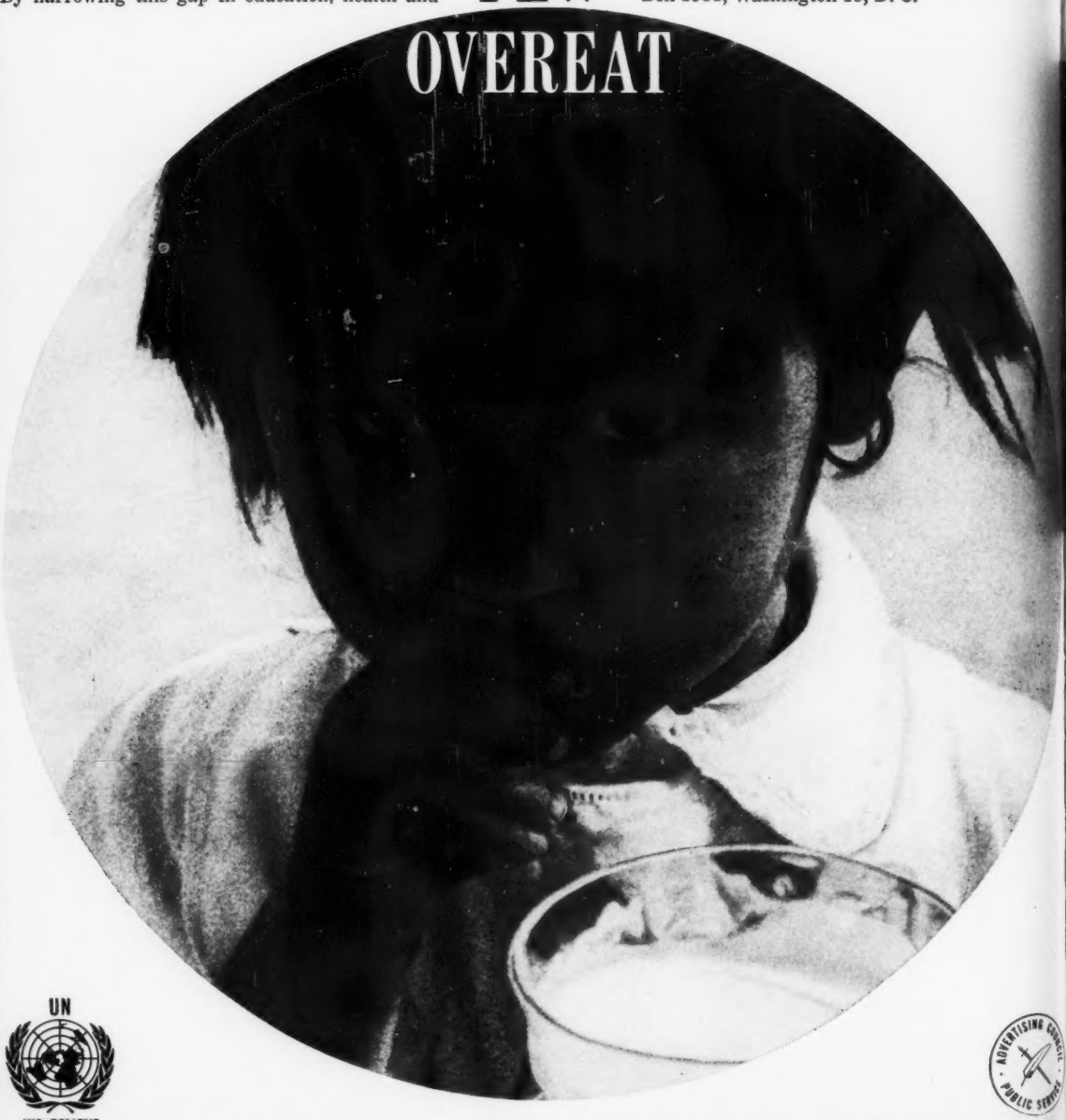

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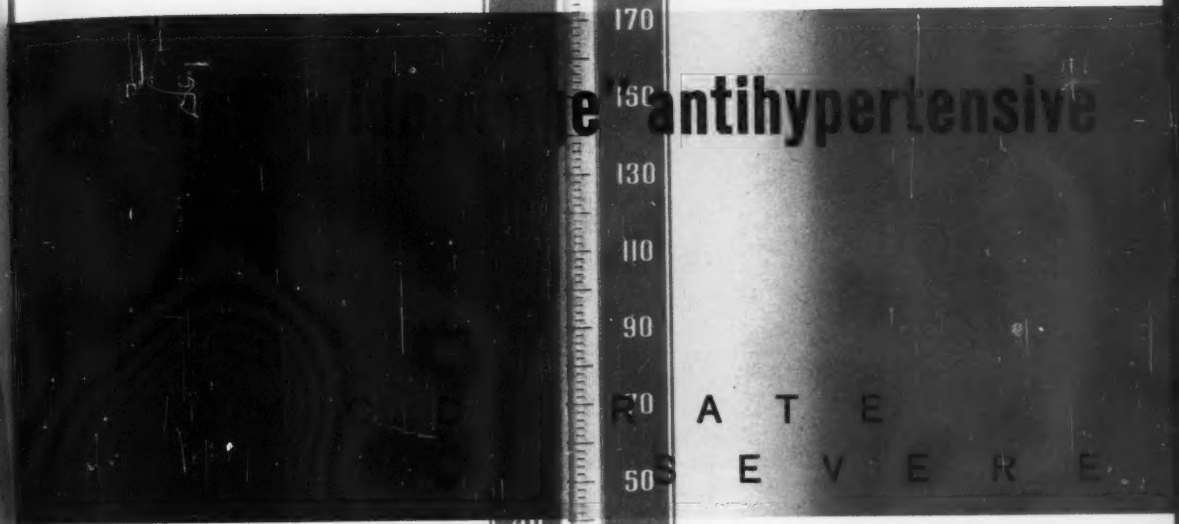


DIUPRES

DIURIL® WITH RESERPINE

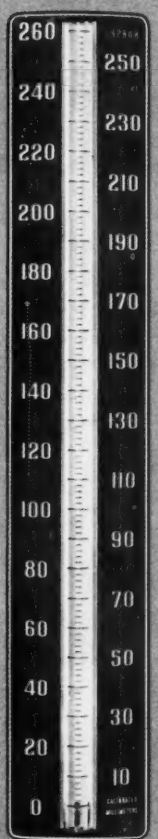
more hypertensives can be better controlled
with **DIUPRES** than with any other agent
... with greater simplicity and convenience

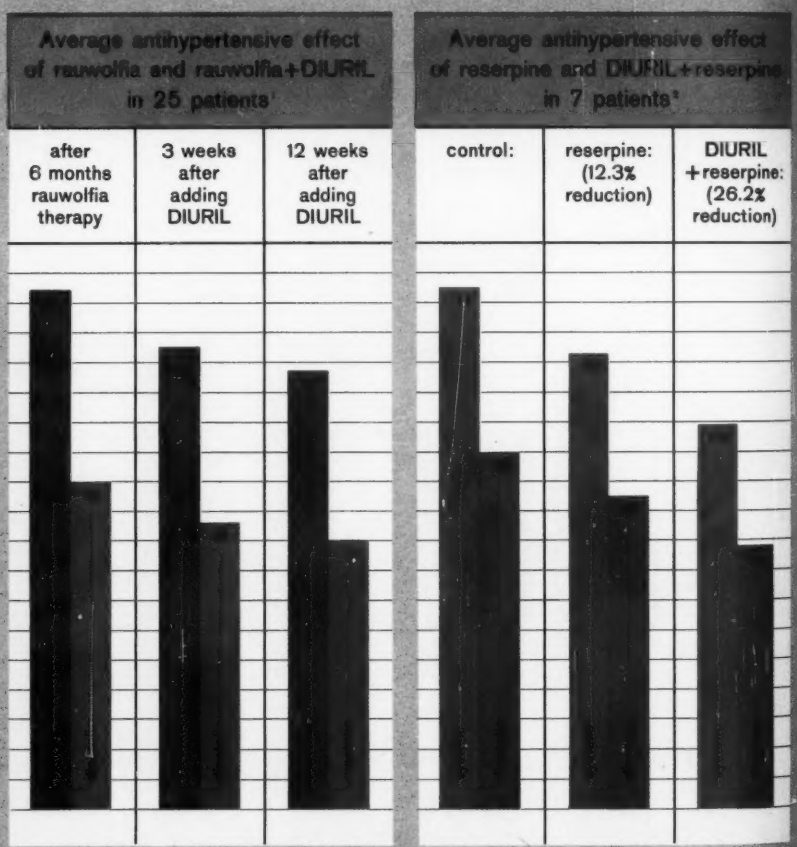
a logical alliance of two antihypertensives
you know and trust provides

increased effectiveness, decreased side effects

potentiated effect

DIUPRES produces an effect greater than either DIURIL or reserpine alone. It is effective in many patients who respond inadequately or not at all to either DIURIL or reserpine.




Average antihypertensive effect of rauwolfia and rauwolfia+DIURIL in 25 patients[1]
after 6 months rauwolfia therapy
3 weeks after adding DIURIL
12 weeks after adding DIURIL
Average antihypertensive effect of reserpine and DIURIL+reserpine in 7 patients[2]
control:
reserpine: (12.3% reduction)
DIURIL +reserpine: (26.2% reduction)

DIUPRES

DIURIL® WITH RESERPINE

effective therapy for most patients

DIUPRES by itself usually provides effective therapy for a majority of patients with mild or moderate hypertension, and even for many patients with severe hypertension. Many patients now treated with other agents which frequently cause distressing side effects can be adequately managed with well tolerated DIUPRES.

provides basic therapy

Should other drugs need to be added to DIUPRES, they can be given in much lower than usual dosage so that their side effects are often strikingly reduced.

rapid onset of effect

The antihypertensive action of DIUPRES is rapidly evident. (Considerable time may elapse before the antihypertensive effect of reserpine alone is observed.)

fewer and less severe side effects

DIUPRES may be expected to cause fewer and less severe side effects than are encountered with other antihypertensive therapy. (Since DIURIL and reserpine potentiate each other, the required dosage of each is usually less when given together as DIUPRES than when given alone. Such reduction in dosage makes side effects less likely to occur.)

often obviates weight gain

DIUPRES minimizes the problem of weight gain seen with reserpine (reserpine alone has been reported to produce weight gain in 50 per cent of patients).[1,4]

virtually eliminates fluid retention

DIUPRES is not likely to cause either clinical or subclinical retention of sodium and water. (Hypotensive drugs, particularly rauwolfia[5] and hydralazine,[6] may cause fluid retention. Even when such retention is subclinical, their antihypertensive effectiveness is diminished.[6])

diet more palatable

With DIUPRES, there is less need for rigid restriction of dietary salt, which patients find so burdensome.

> *"It may well be that the drug* [DIURIL] *produces the benefits of a markedly restricted low sodium diet but without its hardships."*[3]

subjective and objective improvement

DIUPRES allays anxiety and tension, thus reducing the emotional component of hypertension. Organic changes of hypertension may be arrested and reversed. Headache, dizziness, palpitations and tachycardia are usually promptly relieved by DIUPRES. When the *anginal syndrome* accompanies hypertension, the administration of DIUPRES may also cause diminution or even disappearance of this syndrome concurrent with control of the hypertension.

convenient, controlled dosage

Instead of two separate prescriptions, you write one prescription . . . the patient takes one tablet, rather than two different tablets . . . and the dosage schedule is easier for the patient to remember and follow.

> *"patients have fewer lapses and make fewer mistakes in dosage, the simpler the regimen can be made. Therefore I do not hesitate to use more than one medicament combined in one tablet, provided this gives approximately the correct dosage of each."*[6]

economical

DIUPRES will cost the patient less than if he were given two separate prescriptions for its components.

a logical alliance of two antihypertensives
you know and trust provides

increased effectiveness, decreased side effects

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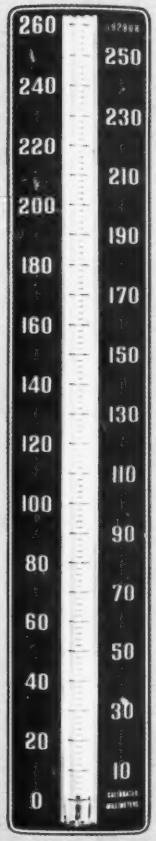

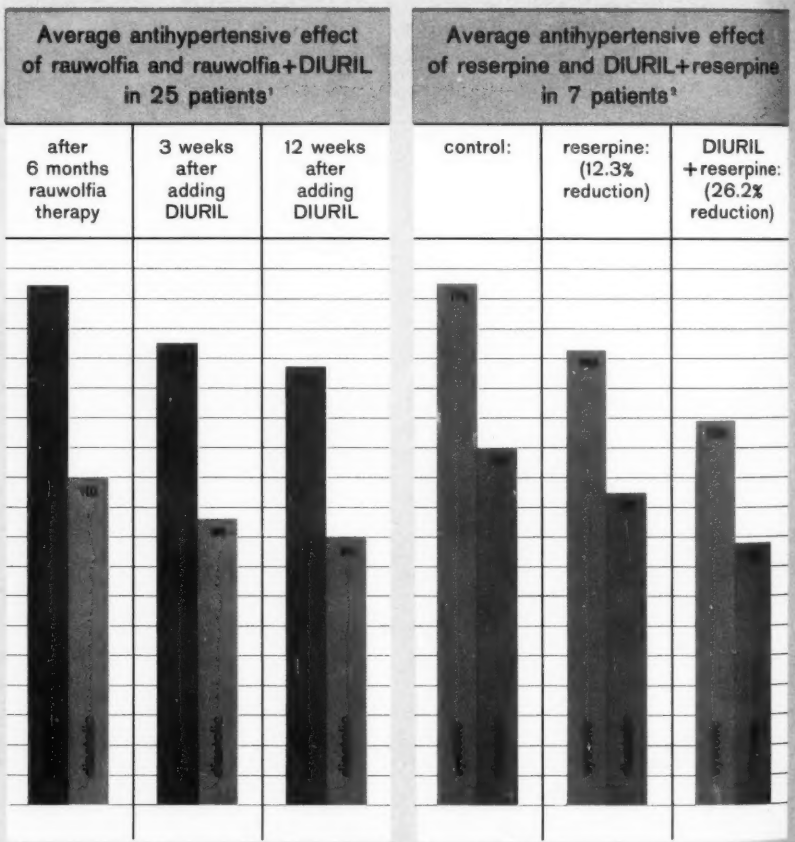
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economical

DIUPRES will cost the patient less than if he were given two separate prescriptions for its components.

Indications:
DIUPRES is indicated in hypertension of all degrees of severity. It can be used in the following ways:

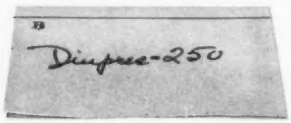
- as total therapy
- as primary therapy, adding other drugs if necessary
- as replacement or adjunctive therapy in patients now treated with other agents

Precautions:
The precautions normally observed with DIURIL or reserpine apply to DIUPRES. Additional information on DIUPRES is available to physicians on request.

Recommended dosage range:
DIUPRES-500—one tablet one to three times a day.
DIUPRES-250—one tablet one to four times a day.
If necessary, other agents may be added.
If the patient is receiving ganglion blocking agents or hydralazine, their dosage should be cut by 50 per cent when DIUPRES is added.

DIUPRES-500

500 mg. DIURIL (chlorothiazide), 0.125 mg. reserpine.
Bottles of 100, 1000.



DIUPRES-250

250 mg. DIURIL (chlorothiazide), 0.125 mg. reserpine.
Bottles of 100, 1000.

the first "wide range" antihypertensive

DIUPRES

DIURIL® WITH RESERPINE

1. Rochelle, J. B., III, Bullock, A. C., and Ford, R. V.: Potentiation of antihypertensive therapy by use of chlorothiazide, *J.A.M.A.* 168:410, Sept. 27, 1958. 2. Freis, E. D., Wanko, A., Wilson, I. M., and Parrish, A. E.: Treatment of essential hypertension with chlorothiazide (Diuril), *J.A.M.A.* 166:137, Jan. 11, 1958. 3. Freis, E. D.: Treatment of hypertension. (Presented at the Annual Meeting of Southern Medical Association, Nov. 13, 1957.) 4. Moyer, J. H., Dennis, E., and Ford, R.: Drug therapy (Rauwolfia) of hypertension, *A.M.A. Arch. Int. Med.* 96:530, Oct. 1955. 5. Perera, G. A.: Edema and congestive failure related to administration of rauwolfia serpentina, *J.A.M.A.* 159:439, Oct. 1, 1955. 6. Wilkins, R. W.: Precautions in use of antihypertensive drugs, including chlorothiazide, *J.A.M.A.* 167:801, June 14, 1958.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

*DIUPRES and DIURIL (chlorothiazide) are trademarks of Merck & Co., Inc.

running noses

and open stuffed noses orally

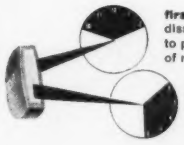
with TRIAMINIC, the oral nasal decongestant

- in nasal and paranasal congestion
- in sinusitis
- in postnasal drip
- in allergic reactions of the upper respiratory tract

safer and more effective than topical medication

- reaches *all* respiratory membranes systemically
- avoids "nose drop addiction"
- presents no problem of rebound congestion
- provides longer-lasting relief

Relief with Triaminic is prompt and prolonged because of this special timed-release action . . . beneficial effect starts in minutes, lasts for hours.


first—the outer layer dissolves within minutes to produce 3 to 4 hours of relief
then—the inner core disintegrates to give 3 to 4 more hours of relief

Each **TRIAMINIC** *Tablet provides:*

Phenylpropanolamine HCl . . .	50 mg.
Pheniramine maleate	25 mg.
Pyrilamine maleate	25 mg.

One-half of this formula is in the outer layer, the other half is in the core.

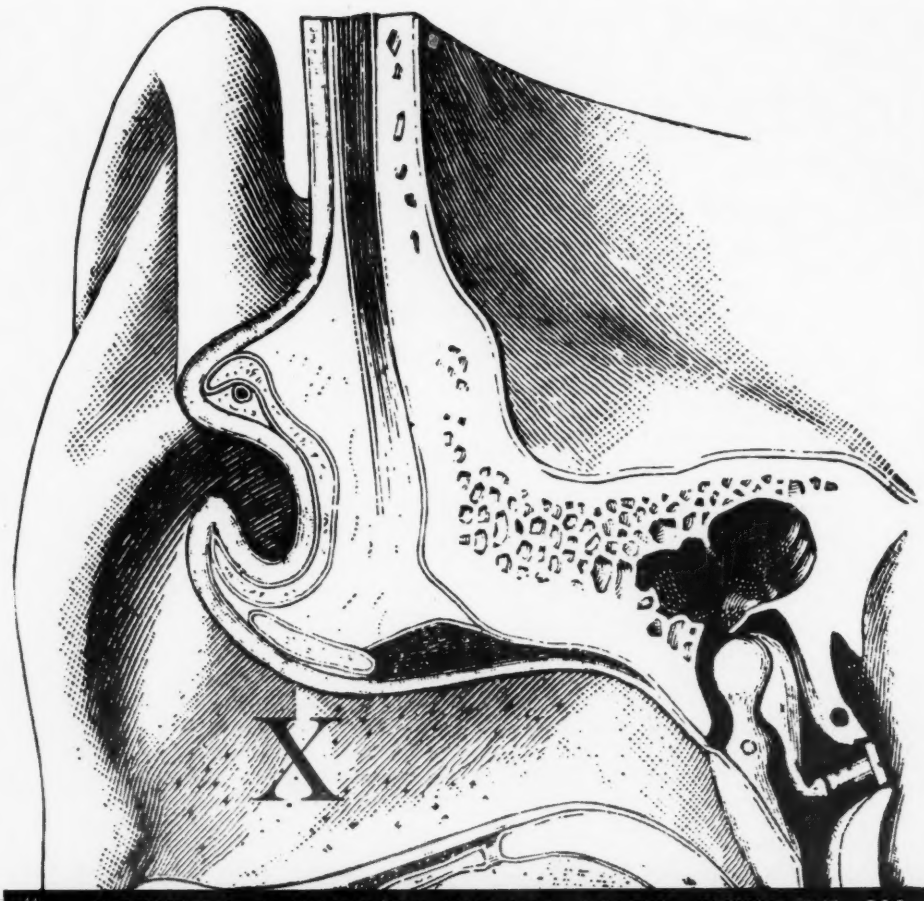
Dosage: One tablet in the morning, mid-afternoon and in the evening, if needed.

Triaminic®

Also available: For the occasional patient who requires only half dosage: timed-release TRIAMINIC JUVELETS. Each Juvelet is equivalent to ½ of a Triaminic Tablet.

For those patients who prefer liquid medication: TRIAMINIC SYRUP. Each 5 ml. tsp. of this palatable syrup is equivalent to ¼ of a Triaminic Tablet.

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada



"...BETTER RESULTS THAN EVER BEFORE IN..."*

OTITIS EXTERNA

AND CHRONIC OTITIS MEDIA WITH

OTOBIOTIC®

ANTIBIOTIC/ANTIFUNGAL EAR DROPS

3.5 mg. neomycin (from sulfate) and 50 mg. sodium propionate per cc. — in 15 cc. dropper bottles.

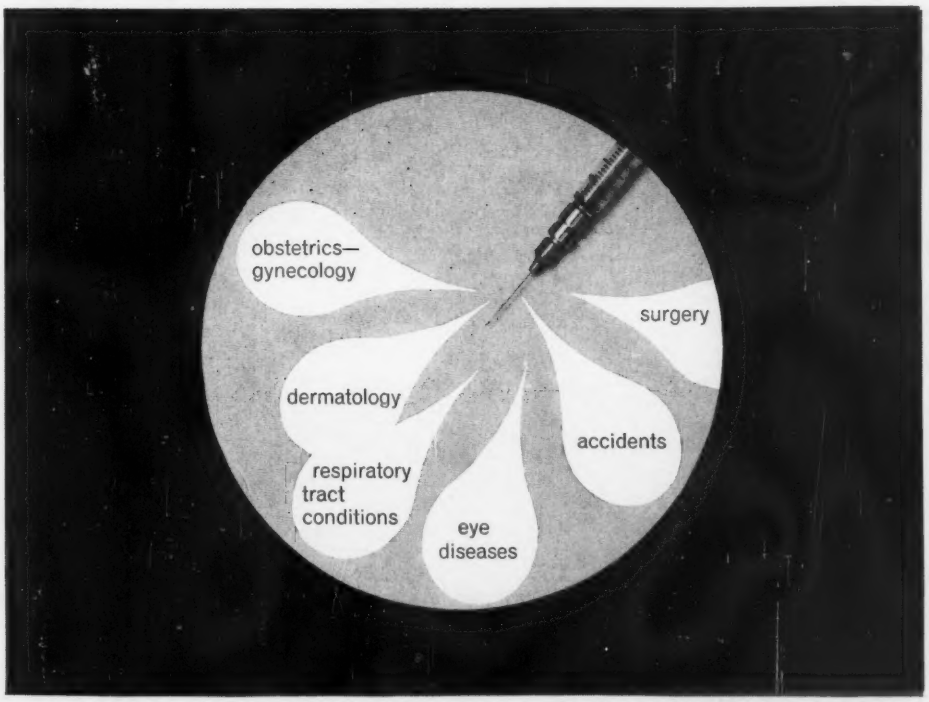
*Lawson, G. W.: Diffuse Otitis Externa and Its Effective Treatment, Postgrad. Med. 22:501 (Nov.) 1957.

AN OTIC SPECIALTY OF WHITE LABORATORIES, INC., KENILWORTH, NEW JERSEY

CHYMAR® **AQUEOUS** is indicated as: # a therapeutic agent —Chymar abolishes inflammation, hastens absorption of edema and blood extravasates, relieves pain, restores impaired local blood and lymph circulation. # a prophylactic agent—Chymar, when given early, suppresses the development of the inflammatory tissue reaction and edema. # an adjunctive agent—Chymar supplements antibiotics in local infections and is useful in inflammatory dermatoses. # Supplied: 5 cc. multiple dose vials. Each ml. contains 5,000 Armour Units of chymotrypsin. Also available—Chymar in Oil.

ARMOUR

PREFERRED FOR SYSTEMIC ANTI-INFLAMMATORY ACTION



ARMOUR PHARMACEUTICAL COMPANY • KANKAKEE, ILLINOIS / *a leader in biochemical research*

Investigator

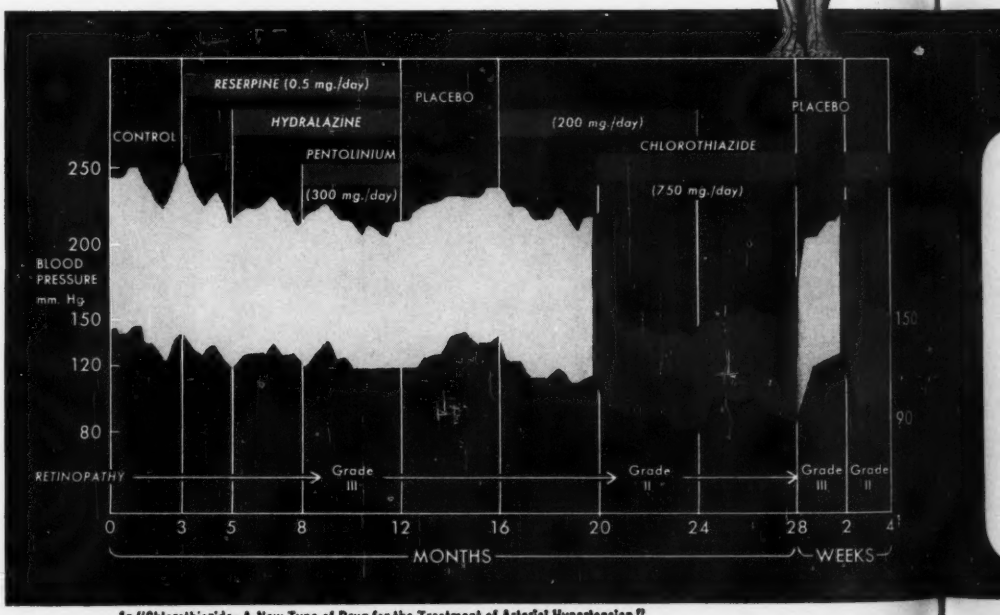
after investigator reports the

Wilkins, R. W.: New England J. Med. 257:1026, Nov. 21, 1957.

"Chlorothiazide added to other antihypertensive drugs reduced the blood pressure in 19 of 23 hypertensive patients." "All of 11 hypertension subjects in whom splanchnicectomy had been performed had a striking blood pressure response to oral administration of chlorothiazide." ". . . it is not hypotensive in normotensive patients with congestive heart failure, in whom it is markedly diuretic; it is hypotensive in both compensated and decompensated hypertensive patients (in the former without congestive heart failure, it is not markedly diuretic, whereas in the latter in congestive heart failure, it is markedly diuretic). . . ."

Freis, E. D., Wanko, A., Wilson, I. H. and Parrish, A. E.: J.A.M.A. 166:137, Jan. 11, 1958.

"Chlorothiazide (maintenance dose, 0.5 Gm. twice daily) added to the regimen of 73 ambulatory hypertensive patients who were receiving other antihypertensive drugs as well caused an additional reduction [16%] of blood pressure." "The advantages of chlorothiazide were (1) significant antihypertensive effect in a high percentage of patients, particularly when combined with other agents, (2) absence of significant side effects or toxicity in the dosages used, (3) absence of tolerance (at least thus far), and (4) effectiveness with simple 'rule of thumb' oral dosage schedules."



In "Chlorothiazide: A New Type of Drug for the Treatment of Arterial Hypertension," Hollander, W. and Wilkins, R. W.: Boston Med. Quart. 8: 1, September, 1957.

MERCK SHARP & DOHME Division of MERCK & CO., Inc., Philadelphia 1, Pa. MSD

'DIURIL' (CHLOROTHIAZIDE)

the effectiveness of

in

Hypertension

as simple as 1-2-3

1 **INITIATE THERAPY WITH 'DIURIL'.** 'DIURIL' is given in a dosage range of from 250 mg. twice a day to 500 mg. three times a day.

2 **ADJUST DOSAGE OF OTHER AGENTS.** The dosage of other antihypertensive medication (reserpine, veratrum, hydralazine, etc.) is adjusted as indicated by patient response. If the patient is established on a ganglionic blocking agent (e.g., 'INVERSINE') this should be continued, but the total daily dose should be immediately reduced by as much as 25 to 50 per cent. This will reduce the serious side effects often observed with ganglionic blockade.

3 **ADJUST DOSAGE OF ALL MEDICATION.** The patient must be frequently observed and careful adjustment of all agents should be made to determine optimal maintenance dosage.

SUPPLIED: 250 mg. and 500 mg. scored tablets 'DIURIL' (chlorothiazide); bottles of 100 and 1,000.

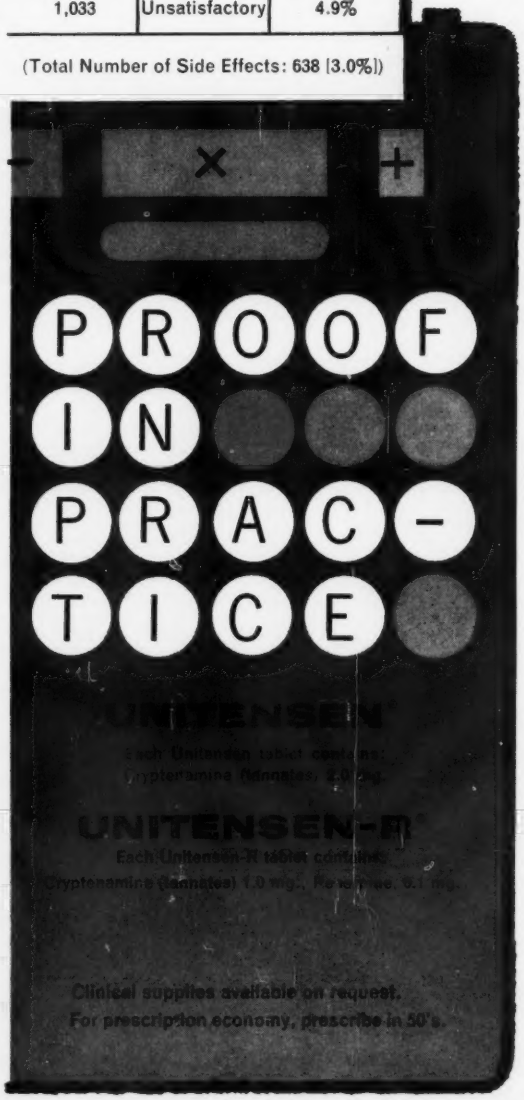
'DIURIL' is a trade-mark of Merck & Co., Inc.

Smooth, more trouble-free management of hypertension with 'DIURIL'

SUMMARY OF REPORTS

No. of Patients	Results	Percent
6,553	Excellent	31.0%
10,843	Good	51.3%
2,703	Fair	12.8%
1,033	Unsatisfactory	4.9%

(Total Number of Side Effects: 638 [3.0%])



A NEW DIMENSION IN RESEARCH

This data deals with the results obtained by 1,988 physicians, treating 21,128 hypertensive patients with Unitensen. The "Proof In Practice" study validates, *in day-to-day private practice*, the findings of clinical trials conducted in hospitals and institutions. It proves that Unitensen affords safe, dependable office management for the majority of hypertensive patients. Unitensen lowers blood pressure . . . improves cerebral and renal blood flow... exerts no adverse effects on circulation . . . and, is virtually free of side effects.

Neisler

Irwin, Neisler & Co.
Decatur, Illinois

Proven

in over three years of clinical use
in over 600 clinical studies

Specific

FOR RELIEF OF ANXIETY
AND MUSCLE TENSION

Selective

Does not interfere with autonomic function
Does not impair mental efficiency,
motor control, or normal behavior
Has not produced hypotension,
agranulocytosis or jaundice

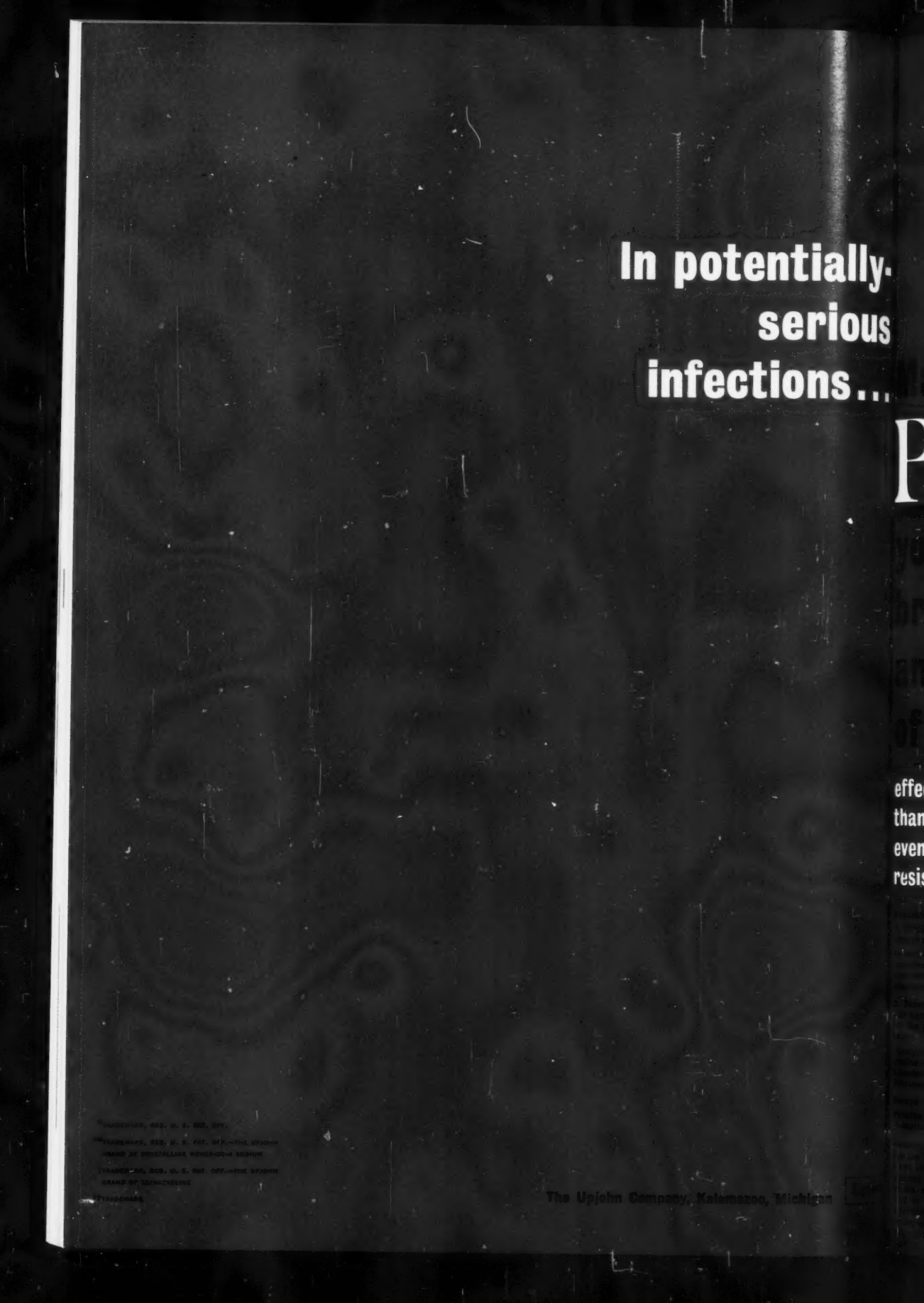
MEPROBAMATE (WALLACE)

Miltown®

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets.

WALLACE LABORATORIES, New Brunswick, N. J.

CH-8043


In potentially
serious
infections...
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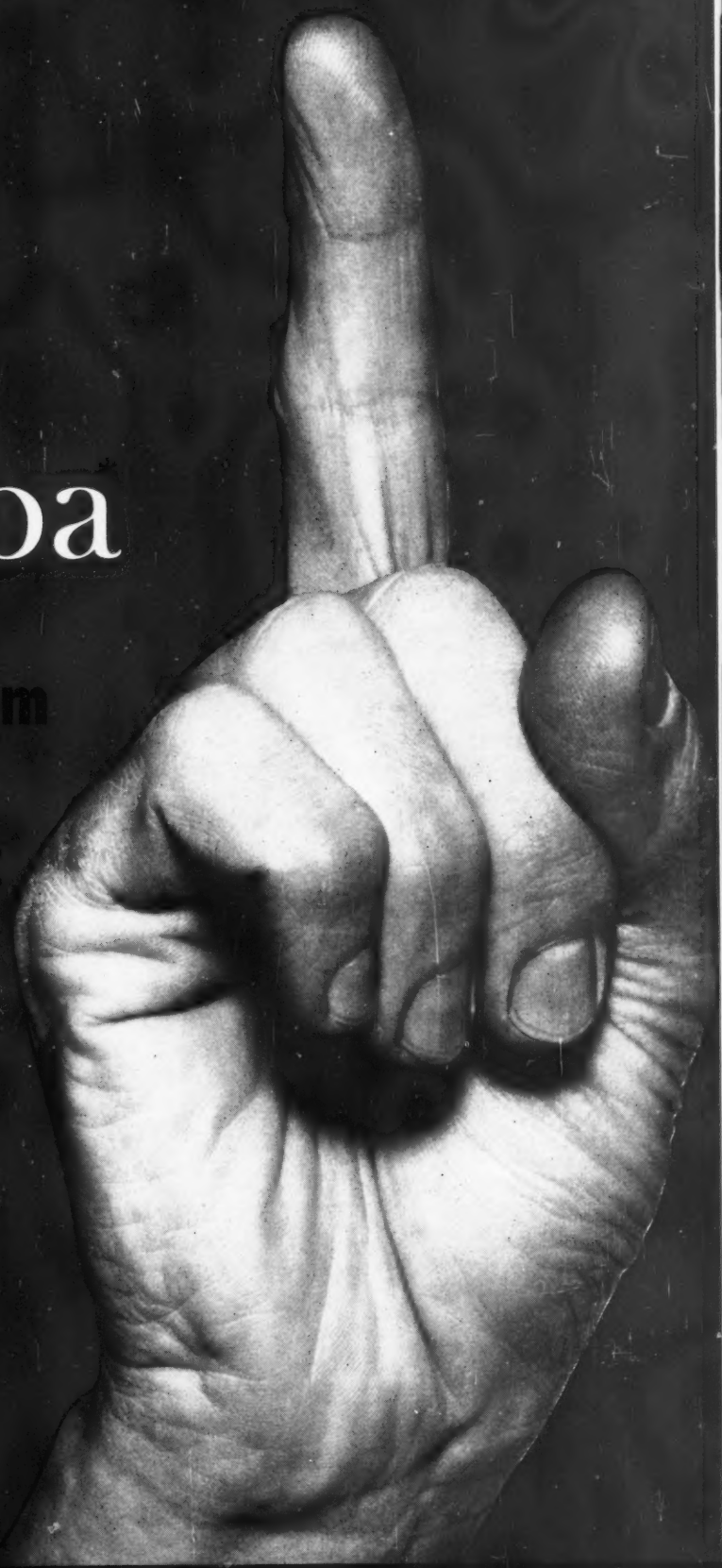
Make new

Panalba

your broad-spectrum antibiotic of first resort

effective against more than 30 common pathogens, even including resistant staphylococci.



POSITIVE EVIDENCE THAT "MEDIATRIC" INCREASES MUSCLE STRENGTH AND ENDURANCE

in less than five months, record of squeeze-bulb test shows repetition frequency increased from 31 to 50 consecutive times in left hand—much improved in right.*

*SQUEEZE-BULB MUSCLE ENDURANCE TEST

Patient A.W., female, age 71

"Mediatric" therapy started at time of first test and continued for 4½ months		Repetition frequency (consecutive times)	
		Left hand	Right hand
1st test	Feb. 16, 1954	31	58
2nd test	July 1, 1954	50	67

improved muscle endurance with steroid-nutritional therapy objectively demonstrated by physical tests

Muscle strength and endurance were determined by stiff-bulb test in a series of older patients before and after "Mediatric" therapy. Improvement was measured by the increase in the number of times a patient could squeeze the stiff bulb at a steady rhythm. Results of this test showed greatly enhanced muscle endurance after continuous "Mediatric" therapy, even in short periods of time.[1] During this period, grip strength of these same patients was measured with a dynamometer, and joint range with a goniometer. These and other physical tests also showed remarkable increase in strength, endurance and coordination.

Such tests have proved to be a valuable and reliable indication of the general improvement in muscle tone and progress that may be obtained with "Mediatric" therapy.

"Mediatric" contains estrogen and androgen in amounts that will help counteract declining gonadal hormone secretion, maintain a positive nitrogen balance, and promote synthesis of protein in muscle, bone and other tissues.

Combining both steroids and important nutritional supplements such as vitamin C, B_{12}, other B vitamins and ferrous sulfate, "Mediatric" brings about increase in physical strength, overcomes general malaise, easy fatigability, lack of interest and vague pains in the bones and joints. In addition, "Mediatric" improves mental outlook and its general "tonic" effect is of especial benefit to your patient.

For better health and vigor in the older patient

"MEDIATRIC"

STEROID-NUTRITIONAL COMPOUND

each capsule or tablet contains:

STEROIDS	
Conjugated estrogens equine ("Premarin")	0.25 mg.
Methyltestosterone	2.5 mg.
NUTRITIONAL SUPPLEMENTS	
Vitamin C (ascorbic acid)	100.0 mg.
Vitamin B_{12} with intrinsic factor concentrate	1/6 U.S.P. Unit
Thiamine mononitrate (B_1)	10.0 mg.
Riboflavin (B_2)	5.0 mg.
Nicotinamide	50.0 mg.
Pyridoxine HCl (B_6)	3.0 mg.
Calc. pantothenate	20.0 mg.
Folic acid U.S.P.	0.33 mg.
Ferrous sulfate exsic.	30.0 mg.
ANTIDEPRESSANT	
d-Desoxyephedrine HCl	1.0 mg.

Suggested Dosages: Male — *1 capsule or 1 tablet daily, or as required.* Female — *1 capsule or 1 tablet daily, or as required, taken in 21 day courses with a rest period of one week between courses.*

Supplied: *Capsules — No. 252 — Bottles of 30, 100, and 1,000. Tablets — No. 752 — Bottles of 100 and 1,000.*

Also available: *"Mediatric" Liquid — No. 910 — Bottles of 16 fluidounces and 1 gallon.*

Ayerst Laboratories • New York 16, N.Y. • Montreal, Canada

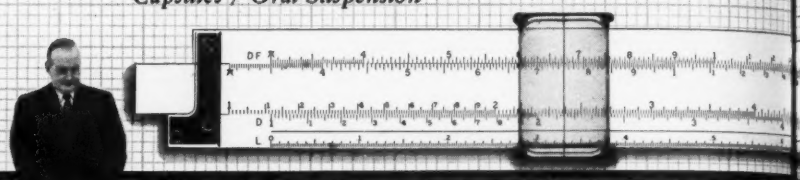
1. Pavlovic, R. M., and Dorizzato, S. M.: Presented before the Third Congress of the International Association of Gerontology, London, England, July 19-23, 1954.

PRONOUNCED TAY-O

℞ Tao* *designed for superior control of common Gram-positive infections*

(triacetyloleandomycin)

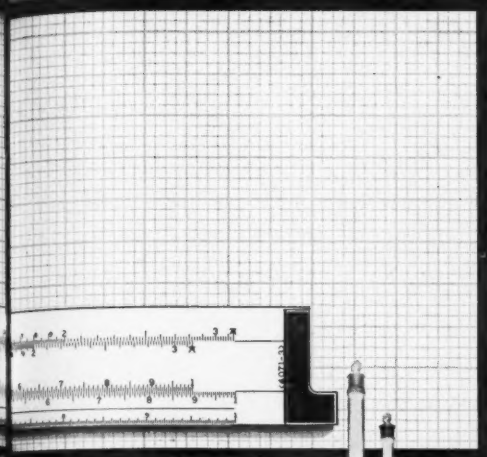
Capsules / Oral Suspension



in the patient:

95% effective in published cases[1-8]

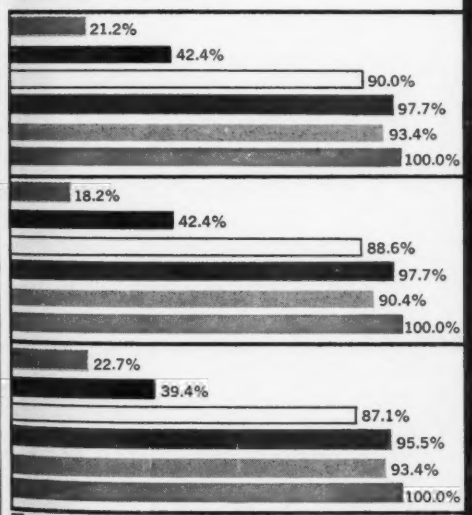
Conditions treated	No. of Patients	Cured	Improved	Failure
ALL INFECTIONS	**558**	[illegible]	**80**	**30**
Respiratory infections	**258**	[illegible]	**31**	**19**
Pharyngitis and/or tonsillitis	65	[illegible]	5	2
Pneumonia	90	[illegible]	17	7
Infectious asthma	44	[illegible]	—	6
Otitis media	31	[illegible]	2	—
Other respiratory (bronchitis, bronchiolitis, bronchiectasis, pneumonitis, laryngotracheitis, strep throat)	28	[illegible]	7	4
Skin and soft tissue infections	**230**	[illegible]	**38**	**1**
Infected wounds, incisions and lacerations	41	[illegible]	8	—
Abscesses	51	[illegible]	8	—
Furunculosis	58	[illegible]	6	1
Acne, pustular	43	[illegible]	15	—
Pyoderma	19	[illegible]	—	—
Other skin and soft tissue (infected burns, cellulitis, impetigo, ulcers, others)	18	[illegible]	1	—
Genitourinary infections	**28**	[illegible]	**3**	**6**
Acute pyelitis and cystitis	10	[illegible]	2	—
Urethritis with gonorrhea or cystitis	8	[illegible]	—	—
Pyelonephritis	4	[illegible]	—	3
Salpingitis	5	[illegible]	1	3
Pelvic inflammation with endometriosis	1	[illegible]	—	—
Miscellaneous (adenitis, enteritis, enterocolitis, subacute bacterial endocarditis, fever, hematoma, staphylococcus carriers, osteomyelitis, tenosynovitis, septic arthritis, acute bursitis, periarthritis)	**42**	[illegible]	**8**	**4**



in the laboratory:

over 90% effective against resistant staph

COMPARATIVE TESTS BY THREE METHODS (DISC, TUBE DILUTION, CYLINDER PLATE) ON 130 STAPHYLOCOCCI[9]



Percentage of organisms inhibited by the range of concentrations listed for each antibiotic.

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References: 1. Koch, R., and Asay, L. D.: J. Pediat., In press. 2. Leming, B. H., Jr., et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 3. Mellman, et al.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 4. Olansky, S., and McCormick, G. E., Jr.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 5. Shubin, H., et al.: Antibiotics Annual 1957-1958, New York, N. Y., Medical Encyclopedia, Inc., 1958, p. 679. 6. Isenberg, H., and Karelitz, S.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 7. Wennersten, J. R.: Antibiotic Med. & Clin. Therapy 5:527 (Aug.) 1958. 8. Kaplan, M. A., and Goldin, M.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958. 9. Truant, J. P.: Paper presented at the Symposium on Antibiotics, Washington, D. C., Oct. 15-17, 1958.

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Southern Medical Journal

PUBLISHED BY SOUTHERN MEDICAL ASSOCIATION

January 1959

The Use of Radioisotopes in the Clinical Study of Renal Function*

JULIAN D. BOYD, M.D., *Huntington, W. Va.,* LESLIE A. MORGAN, M.D., *Miami* and *Coral Gables, Fla.,* and ALVIN BLUM, B.S., *Coral Gables, Fla.*

Here is a new method of determining renal function which offers most interesting potential uses in the study of renal physiology and of renal disease.

RENAL FUNCTION STUDIES employing Diodrast tagged with radioiodine were first described by Winter[1] in 1956. The method he described is based on the manner of excretion of Diodrast by the kidney. From his report it was evident that this new test has certain advantages over some other tests commonly used for testing renal function. At this hospital we have been using the test on selected subjects since April, 1957. To date, more than 125 tests have been performed. This report is designed to show the types of curves or radiorenograms which have been obtained from patients with a variety of different renal abnormalities, as contrasted with those from patients with normally functioning kidneys, and to indicate briefly the manner in which the radiorenogram is to be interpreted.

Method

Basically the test depends on the intravenous injection of an extremely small amount of Diodrast which has been tagged with radioiodine,* then obtaining a graphic record of the rate which the material is accumulated concurrently in each kidney, and of its subsequent excretion. The test requires from 15 to 20 minutes for its completion once the injection has been made.

The amount of Diodrast employed is infinitesimal compared with the amount used for the conventional intravenous urogram: 0.4 mg. as contrasted with 15 Gm. This is no more than the amount of Diodrast given as a preliminary test for sensitivity prior to urography. The amount of radioactivity inherent in the injected material likewise is negligible: about 4 microcuries for each 10 kg. of body weight. The usual roentgenogram of the chest entails a hundred times this exposure, the urogram, even more. Before administration the material as it is received is diluted to a concentration of about 20 microcuries for each milliliter. The radioactivity within the kidney and its surrounding structure is measured through the use of two scintillation detectors, one placed over each kidney. Each detector is circuited through a separate rate meter, and from the latter to paired rectilinear recording milliammeters. The scintillation detectors are held rigidly in a support, as described by Winter, in such a position that each detector will "see" the radioactivity coming from the respective kidney with a minimal inclusion of radioactivity from adjacent structures, especially from the liver. This is accomplished by directing the axis of the detector from above downward at an angle of about 30 degrees with the body axis, depending on the body build. The patient is seated, leaning slightly forward.

Definition of the Normal Radiorenogram

The pattern of change in radioactivity over the normal kidney may be considered in three

*Read before the Section on Pathology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

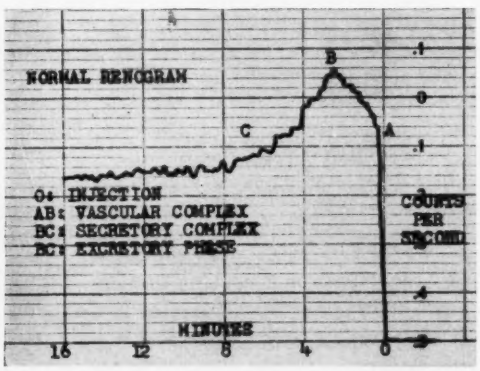
†From the Veterans Administration Hospital, Coral Gables, Fla.

*The Radiodiodrast was obtained from Abbott Laboratories.

stages. Immediately after injection, the material becomes distributed throughout the blood stream, and a radiation detector over any vascular region would demonstrate a sudden rise in radioactivity. Next, the Radiodiodrast is concentrated in the kidney as it is secreted by the renal tubules. Then almost concurrently, the drainage of the Diodrast is rapid, causing the concentration of radioactivity to be lessened as the urine leaves the kidney. When the tubular secretion rate equals the rate of removal, the peak of the curve will be reached. As the rate of drainage surpasses the rate of maximum tubular secretion the curve will decline, rapidly at first, gradually reaching a plateau.

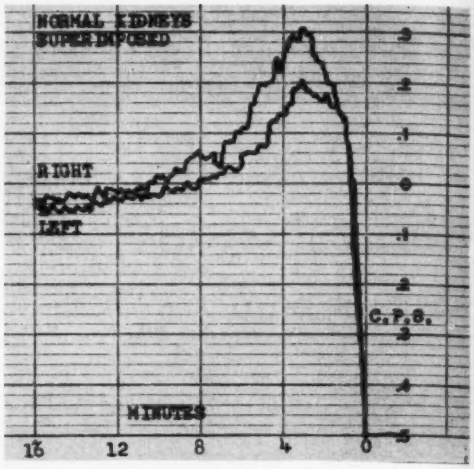
Over the normal kidney the process described will yield a radiorenogram similar to that shown in figure 1. The curve begins at the right and progresses to the left. The horizontal coordinate is graduated in terms of time. The vertical coordinate represents the magnitude of radioactivity, based on the number of counts each second; it is not expressed in absolute units. Point *O* indicates the moment when the tagged Diodrast was injected intravenously. The segment *OA* represents the almost immediate rise in blood concentration of the material. Segment *AB* represents the accumulation of Diodrast in the kidney over and above the concentration in the blood and surrounding tissues. Point *B* represents the moment when the accumulation is maximum and is equalled by the drainage rate. Segment *BC* reflects the dominance of drainage over accumulation. Typically, segment *OA* is very abrupt. It varies with the time setting of the recorder. *AB* shows a sharp upswing over point *A*, with gradual deceleration. Usually the first portion of segment *BC* falls rather sharply, then approaches a plateau terminating at a level similar to that of point *A*. This plateau usually is reached within 10 to 12 minutes after injection, or may be attained more slowly.

FIG. 1



Normal radiorenogram from single kidney, showing components of the curve. Progression is from right to left. Horizontal coordinates express time lapse after intravenous injection of I^{131} tagged Diodrast. Vertical coordinates indicate relative increase in radioactivity of the region. OA represents the vascular complex; AB the secretory complex; BC the excretory phase.

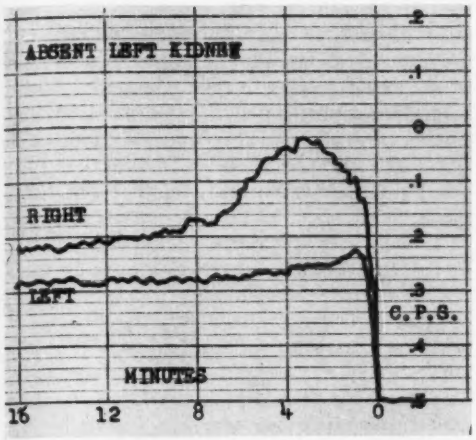
FIG. 2



Superimposed radiorenograms of normal right and left kidney.

Qualitatively, the simultaneous curves for a normal pair of kidneys will be similar. The height of the two curves may vary without indicating abnormality or difference of function. The curve for the right kidney frequently is higher from point *A* through *C* than for the left kidney, due to the fact that the liver too may pick up Diodrast, though at a slower rate than does the kidney, and this concentration may be included in the field "seen" by the scintillation detector. By the administration of some nonradioactive "carrier" Diodrast, the apparent right renal dominance may be eliminated.[2] The absolute height of the curve likewise will be determined in part by the setting of the machine, the amount of tissue which separates the scintillation detector crystal from the kidney, and the administered dose. Figure 2 shows the superimposed recordings made from a pair of presumably normal kidneys.

FIG. 3



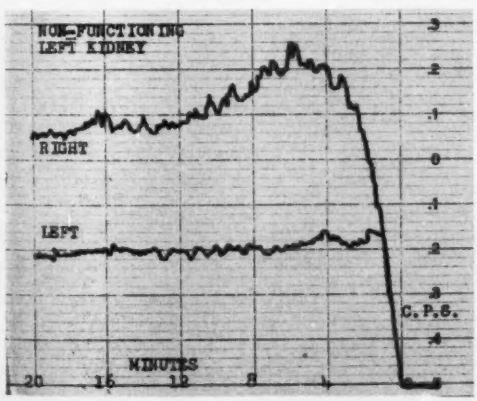
Superimposed radiorenograms: right kidney normal, left kidney surgically removed.

Modification of the Radiorenogram Observed with Disturbances of Renal Function

The illustrations which follow show the types of curves which have been observed in patients with various types of renal disease.

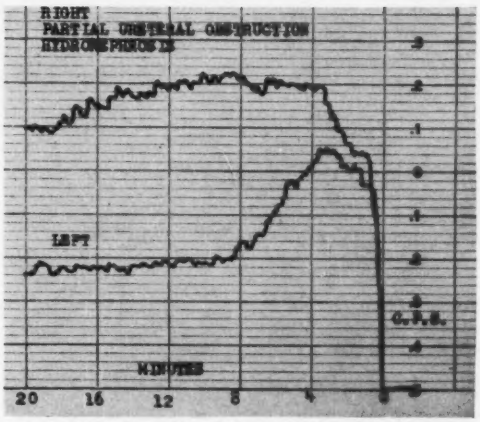
Figure 3 was made from a patient with but one kidney. A left kidney and ureter had been removed many years earlier because of a suspected papillary ureteral tumor. The curve from the right kidney is interpreted as normal. The *OA* segment from the curve obtained over the left renal region is indistinguishable from that for the right, but the left *AB* component shows no upswing. This left renogram typifies the findings when there is no renal function present. Another example is seen in figure 4; here the left kidney although present is nonfunctioning. This patient had severe hypertensive cardiovascular disease which was unresponsive to all medical treatment. We have seen 7 additional patients with hypertension whose records indicated a nonfunctioning kidney.

FIG. 4



Superimposed radiorenograms: right kidney normal, left kidney nonfunctioning; patient had severe hypertensive cardiovascular disease.

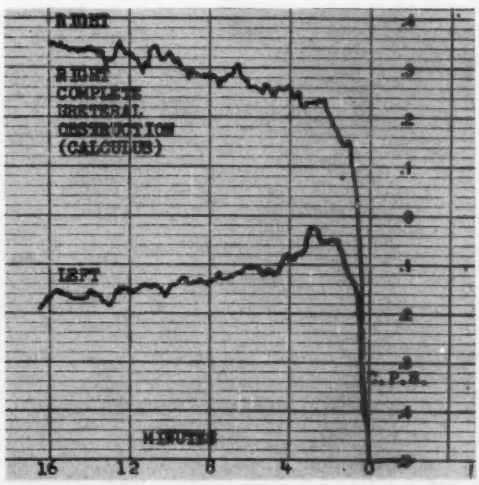
FIG. 5



Superimposed radiorenograms: left kidney normal, drainage from right kidney obstructed with hydronephrosis present.

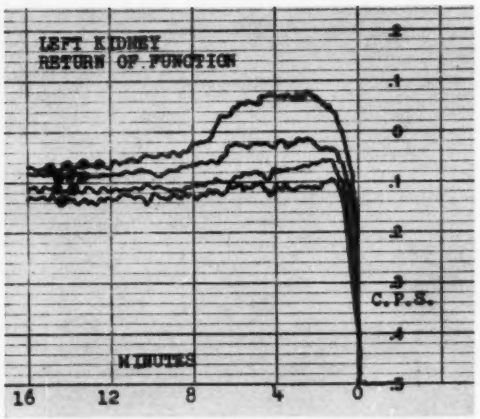
The patient portrayed by figure 5 had hydronephrosis on the right side, visualized by urography, with partial ureteral obstruc-

FIG. 6



Superimposed radiorenograms: left kidney function possibly impaired; drainage from right kidney completely obstructed due to ureteral calculus.

FIG. 7



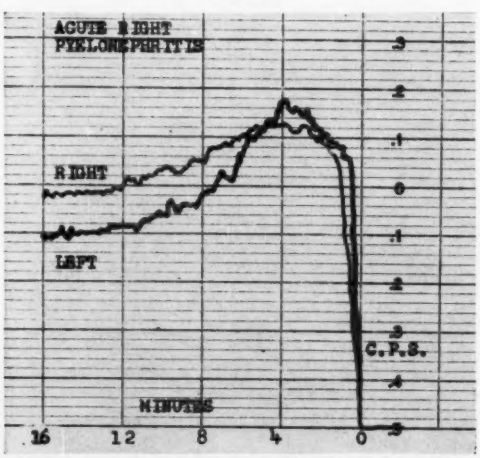
Superimposed serial radiorenograms of left kidney with prolonged ureteral obstruction due to calculus. The curve marked with a single dot was made prior to lithotomy; the curves with 2, 3 and 4 dots were made respectively on the first, second and fifth days after lithotomy.

tion and a past history of nephrolithiasis. The left radiorenogram is considered normal. That on the right appears normal in the *OA* and *AB* segments, but the *BC* segment reflects lack of drainage from the upper collecting system. Figure 6 offers similar evidence of obstruction of renal drainage but of greater degree. This patient was being evaluated for a possible abdominal aneurysm, and had had a normal intravenous pyelogram 2 weeks previously. This record was obtained after the onset of abdominal pain and vomiting. A calculus was passed one week later. Note that the curve continued to rise throughout the entire period of the test.

Figure 7 shows the serial radiorenograms of the left kidney from a patient who had a stone removed from the left ureter after prolonged obstruction. The curve made prior to lithotomy is marked by a single dot. The other three curves with 2, 3 and 4 dots were made respectively on the first, second and fifth day after lithotomy. These records are interpreted to show loss in accumulating function associated with urinary blockage, which was not relieved immediately after lithotomy. Only on the record of the fifth day does the curve approach the normal. It is worthy of emphasis that this delay in restitution of normal kidney function was not shown by the intravenous urograms which were made concurrently. It is reasonable to assume that prolonged blockage of renal drainage may impair the accumulating function of the kidney.

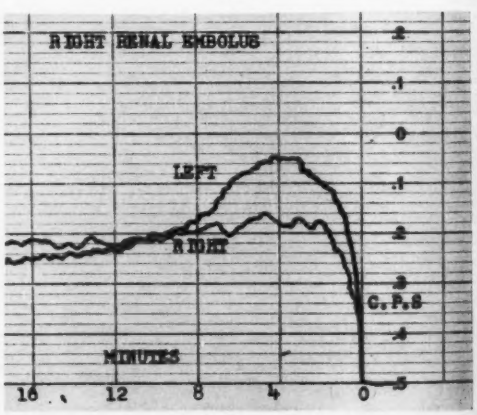
Additional examples of impairment of renal function are shown in the next few illustrations. Figure 8 reflects a minor disturbance of function in the right kidney in a patient with acute right pyelonephritis. The record is modified by the presence of slight ptosis of that kidney. Figure 9 was obtained from a 30 year old man who was in marked congestive heart failure with persistent auricular fibrillation. Eleven days after admission he was awakened suddenly by severe pain in the right upper quadrant at the costovertebral angle. A clinical diagnosis was

FIG. 8



Superimposed radiorenograms from two kidneys in a patient with acute right pyelonephritis and slight ptosis.

FIG. 9



Superimposed radiorenograms from a patient with right renal embolus.

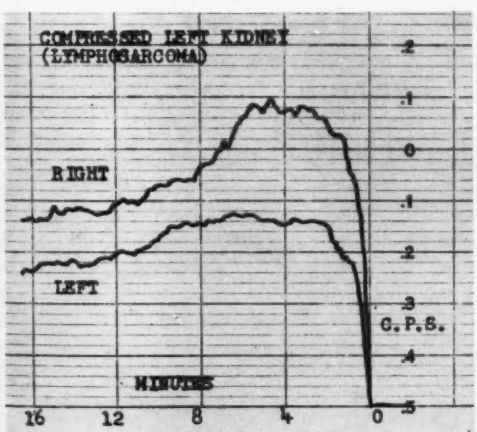
made of right renal embolus. The patient portrayed by figure 10 had compression of his left kidney by a large extrarenal mass; all urinary studies were normal. Finally, figure 11 shows marked reduction of renal function in a 29 year old white woman with bilateral chronic pyelonephritis and associated contracted kidneys. This patient's renograms show little more renal function than observed in patients with unilaterally nonfunctioning or absent kidneys.

Discussion

The radiorenogram has several virtues which recommend its use as a test for renal function. The test requires no special preparation of the patient. It is rapid, safe, relatively inexpensive, and the results are immediately available. There is no radiation hazard from the minute amount of radioactivity administered. The test is not recommended as a replacement for the intravenous urogram or for other accepted tests, but instead as a supplementary diagnostic procedure or as a screening device.

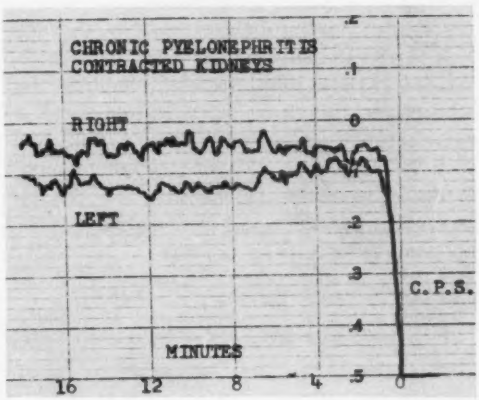
The normal kidney yields a radiorenogram which is easily recognized as conforming to normal standards. In the presence of disturbed renal function, the renogram is altered in such a manner that information of value may be deduced as to the secretory capacity of the respective kidney, and as to the drainage of the organ. Additional study will be needed to establish any correlation as to the relative vascularity of the kidney.

FIG. 10



Superimposed radiorenograms from a patient with left kidney compression due to extrarenal retroperitoneal mass (lymphosarcoma).

FIG. 11



Superimposed radiorenograms from a patient with chronic nephritis and bilaterally contracted kidneys.

The test requires less than half an hour for its completion, once the patient has been positioned for the test and the tagged Diodrast has been injected intravenously. Usually, adequate information can be made available within 15 minutes.

The dose of Diodrast needed for the test is so small that little or no attention need be paid to the possibility of the patient being sensitive to the material.

The amount of radiation received by the patient similarly is negligible. Moreover, of the radiation received, only minimal amounts reach the gonads, in contrast to the gonadal exposure which may result from intravenous urography.[3]

Because of the low dose of Diodrast and of irradiation, and because of the rapid clearance of the injected Diodrast by the kidneys, it is possible to repeat the radiorenographic procedure at rather frequent intervals, and as often as the circumstances require. This feature of the test not only recommends its use for clinical observations of patients with organic or functional disorders of the kidneys; it also makes it useful for physiologic studies of the variability of renal function under imposed conditions of load.

The simplicity, speed and economy of the radiorenographic technic recommend the test as a routine screening procedure where renal disease should be ruled out. It has been

suggested that the test be used wherever hypertension is present, to distinguish those patients who have unilateral disease.

It is recognized that the test's use will be limited to those hospitals where facilities and equipment for the clinical employment of radioisotopes are available. The provision of such facilities as a part of modern hospitals is becoming so prevalent that the test deserves consideration as one of the routine hospital laboratory procedures.

Summary

The study of renal function through radioisotope technics by means of I^{131} tagged Diodrast is described, and typical radiorenograms in health and disease are presented. The simplicity, speed, safety and definitive nature of results of the test recommend its employment as a screening agency and as a supplement to other tests for renal function now commonly employed.

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Superficial and Deep Mycoses in Cuba:

A Report Based on 1,174 Cases*

V. PARDO-CASTELLO, M.D., and FERNANDO TRESPALACIOS, M.D.,†
Havana, Cuba

The authors describe the mycoses encountered in Cuba as related to the etiologic organisms.

THIS IS A CLINICAL REPORT on 1,174 cases of superficial and deep mycoses seen at the Clinic for Dermatology of the University Hospital in Havana. In most of these cultures were successfully made and classified. We include here 50 cases of pityriasis versicolor, erythrasma and trichomycosis palmellina, but no cultures were obtained from these cases when planted in various culture media.

Table 1 shows the incidence of these parasitic conditions and their relative frequency.

Superficial Mycoses

Tinea of the scalp. Of the 249 cases, 182 were caused by *M. canis,* 56 by *T. tonsurans,* 3 by *T. mentagrophytes,* 5 by *M. gypseum* and 3 were mixed, *T. tonsurans* and *M. canis.*

Kerion complication was observed in 13 cases of *M. canis,* 2 cases of *T. mentagrophytes,* 2 cases of *M. gypseum* and 2 cases of *T. tonsurans.*

Of the cases of tinea of the scalp, 168 were in males and 81 in females; 199 were white and 50 were colored; 176 were city dwellers and 73 came from rural areas.

The youngest patient was one month old. The others were between 9 and 15 years old, except for 2 cases in adults, a woman of 20 and a man of 65 years. The patient of 20 was from a farming district; she had almost complete alopecia of the scalp and widespread scaly tinea of the glabrous skin. She had had the condition since childhood, and therapeutic measures, including vaccines and all the local treatments, were of no avail. In this case *T. tonsurans* was recovered from both the scalp and the glabrous skin. The patient who was 65 years of age was also from a farming area, and the offending organism was *M. gypseum.* In this case the disease was limited to the scalp. Both patients were white (Fig. 1).

In several cases of tinea of the scalp in children, there also were cutaneous lesions. One patient with kerion caused by *T. mentagrophytes* also had inflammatory kerion-like lesions of the skin on the right forearm and right thigh, and phytids of hands and feet. This case responded favorably and rapidly to injections of penicillin. (This has been our experience with all cases of kerion as well as of inflammatory sycosis of the beard and mustache. The pyogenic complication loosens the hairs, and when penicillin cures this condition the hairs fall out and consequently the parasitic condition is cured as well. In one case the condition was clinically diagnosed as "folliculitis et perifolliculitis abscedens et suffodiens," cultures showed *T. tonsurans.* Treatment with penicillin intramuscularly as well as aqueous penicillin injected *in situ,* caused a rapid disappearance of the lesions in the course of about 2 weeks.) Ramos e Silva[1] has reported 14 cases of this condition

TABLE 1

		Number of Cases	*Percentage*
1.	Tinea of the scalp	249	21.2
2.	Tinea cruris	227	19.4
3.	Dermatophytosis of feet	206	17.5
4.	Onychomycosis	144	12.3
5.	Tinea of the glabrous skin	78	6.6
6.	Chromoblastomycosis	71	6.0
7.	Candidiasis	64	5.5
8.	Parasitic sycosis of beard	41	3.5
9.	Intertriginous dermatophytosis	11	0.9
10.	Sporotrichosis	10	0.8
11.	Tinea nigra palmaris	8	0.7
12.	Actinomycosis	7	0.6
13.	Mycetoma of feet (Nocardiosis)	5	0.5
14.	Mycetoma of feet (Monosporiosis)	1	
15.	Parasitic sycosis of eyebrows	2	0.2
16.	Pityriasis versicolor, Erythrasma, Trichomycosis palmellina (no cultures)	50	4.3

*Read before the Section on Dermatology and Syphilology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

†From the Department of Dermatology, "Calixto Garcia," University Hospital, Havana, Cuba.

FIG. 1

Diffuse tinea of the scalp due to *M. canis.*

from which cultures of *T. tonsurans* were obtained 8 times, *T. mentagrophytes* twice and an unclassified trichophyton once. In our cases of kerion, *M. canis* was recovered 13 times, *M. gypseum, T. mentagrophytes* and *T. tonsurans,* once each. *M. audouini* has not been reported in Cuba.

The etiologic agents of tinea of the scalp in the different countries of the Americas varies. In Canada, Davidson and Gregory[2] found *M. audouini* and *M. canis* almost equally frequent, with 54 cases of the former and 49 of the latter.

In the United States, Franks and Taschdjian[3] reported *M. audouini* as the most common agent in tinea of the scalp, followed by *M. canis, T. tonsurans, T. schonleinii, T. violaceum* and *T. gypseum.* Polsky[4] finds that in Texas *M. canis* is the most frequent, followed by *M. audouini, T. mentagrophytes* and *M. gypseum,* with *M. canis* leading almost 5 to 1 over *M. audouini.* Lehman, Pipkin and Ressmann,[5] also from Texas, have reported the incidence of etiologic agents for tinea capitis as follows: *M. canis* 53%, *M. audouini* 11%, *M. gypseum* 4%, *T. mentagrophytes* 14%, *T. tonsurans* 11% and *T. violaceum* 2 per cent.

In Argentina, Negroni[6] found, in 615 cases of tinea of the scalp, 458 or about 75% were caused by microsporia, 23% were caused by trichophytia and about 2% by favus.

In Belfast, Northern Ireland, Beare and Chesseman[7] found that the predominating agent of tinea of the scalp was *M. audouini,* about 80% of the cases against slightly over 20% for the rest of the dermatophytes in the following order: *M. canis, T. sulfureum, T. discoides, T. mentagrophytes, T. equinum* and *A. schonleinii.*

Tinea of the scalp in adults is infrequent and almost rare. However, if systematically investigated it might be found in a larger proportion of cases. Tinea in adults tends to be of diffuse distribution and not confined to medallion-like areas, as is commonly seen in children. Kerion has also been reported several times in adults by Fox,[8] in 1926, in a woman aged 25, due to *M. audouini,* and by Cummer,[9] in 1937, in a man, caused by *M. gypseum.* Pipkin's[10] contribution of 57 cases of tinea of the scalp in adults showed the necessity of increasing the index of suspicion in chronic cases of dry dandruff (Fig. 2).

In Puerto Rico, Torres and Georg[11] have reported a case of tinea of the scalp caused by *T. gallinae.*

The soil and the skin, hairs and feathers of animals are natural reservoirs for the dermatophytes. Pathogenic dermatophytes have been recovered from soil and from animals

FIG. 2

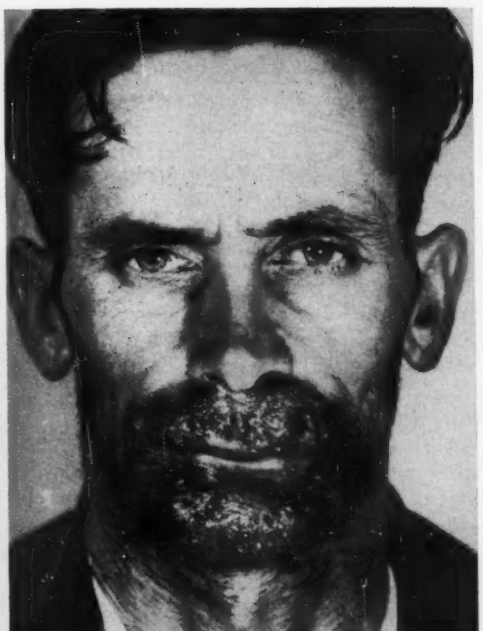
Tinea of the scalp and alopecia due to *T. tonsurans* in an adult.

by Ajello,[12] Emmons,[13] Gordon,[14] Vogel and Timpe,[15] Kaplan and Georg,[16] and others in the United States and by Fuentes[17] in Cuba.

One remarkable and iconoclastic contribution to the recent literature on dermatophytes, is that of Paldrok,[18] who claims that there are only three species of dermatophytes, i.e., *M. audouini* (former *M. canis*), *M. gypseum* and *M. tonsurans*, (former *T. mentagrophytes*), and that all other species described are degenerative states of these three. These conclusions were drawn by the author after growing a large number of dermatophytes at different temperatures from 6 to 44° C. at the Karolinska Institut of Stockholm. Paldrok's work deserves consideration and should be repeated by mycologists everywhere.

With the newer more active antifungal preparations, aided by manual depilation, if necessary under the Wood light, most tineas of the scalp can be cured in four to six weeks. Tineas due to *T. tonsurans* and *T. mentagrophytes* are sometimes more stubborn. We do not epilate by means of x-rays except in very exceptional cases,—those proving stubborn after some weeks of local treatment (Fig. 3).

FIG. 3



Sycosis of the beard and mustache due to *T. mentagrophytes.*

Tinea cruris. Of the 227 cases of tinea cruris, 219 were caused by *T. rubrum*, 3 by *T. mentagrophytes*, 2 by *T. tonsurans*, 2 by *M. gypseum* and 1 by *E. floccosum.*

The great majority of cases, 175 were seen in patients between 21 and 60 years of age, and only 3 cases in children. There were 141 cases in men and 86 in women; 179 were in white and 86 were in colored patients. Although the crural areas were usually affected in most cases, the condition spread beyond this area to the gluteal and pubic regions, to the torso, the extremities and even to the face in 14 patients.

Two cases caused by *T. mentagrophytes* and 2 caused by *M. gypseum* were of highly inflammatory lesions. All 4 patients were from rural areas.

It is said by Higuchi[19] that the scrotum is seldom affected by trichophyton. In our experience itching and scaliness of the scrotum in cases of tinea cruris happen very frequently. However, we have not been able to recover any of the etiologic fungi in cultures from the skin of the scrotum.

Tinea of the eyebrows. Two children, 6 and 10 years of age, had scaliness and broken hairs of the eyebrows with partial loss of hair; there was no tinea of the scalp or of the skin. *M. canis* was recovered in pure culture in both cases. One was a city child and the other came from a rural area.

Beare, Martin and Cheeseman[7] have reported 3 cases of tinea of the eyebrows due to *M. audouini* and one of tinea of the eyelashes due to *M. canis.* In these cases there was also coincidental tinea of the scalp or of the skin.

Onychomycosis. Of the 144 cases of onychomycosis, 137 were due to *T. rubrum* and 7 to *C. albicans.* Many of the patients also had tinea cruris or dermatophytosis of the feet, some had both conditions. Over 98% of these patients were between the ages of 20 and 60; one child 9 years of age had onychomycosis of the fingers and toes. Finger nails were affected in 83 cases, toe nails in 35, and both finger and toe nails in 26 cases. There were 67 men and 77 women in this series.

Treatment of onychomycosis is rather protracted; several months are often needed to

cure most patients, and commonly both patient and dermatologist become discouraged. However, softening with salicylic acid plaster and mechanical removal of the softened nail plate, followed by antifungal treatment is the best method of treatment. It takes 4 to 6 months to effect a cure. There are many successful antifungal preparations, such as tincture of iodine, copper undecylanate, salicylanilide, mono- and dichloro-salicylanilide, undecylenic acid, zinc undecylanate, which in different combinations in nongreasy creams or in powder form are quite effective in the treatment of these conditions. We insist on the previous use of 40% salicylic acid plaster for at least 4 days, followed by mechanical removal of the softened nail plate, before applying the antifungal preparations under a closed dressing. Change of the local dressing is done every 2 or 3 days.

Onychomycoses due to aspergilli and penicillia are not rare, but there is always the possibility of growth of these organisms as saprophytes on injured and dead nails. One unusual case has been reported by Bleil[20] of onychomycosis due to *M. audouini.*

The cases of onychomycosis due to *C. albicans* were unusually few in our series. Another unusual feature of our group of cases is the large proportion of onychomycosis of the finger nails over those cases affecting the toe nails.

Dermatophytosis of the feet. Squamous, vesicular, macerated and hyperkeratotic dermatophytosis of the feet were diagnosed in 206 cases. The etiologic agents recovered were *T. rubrum* in 73 cases, *T. mentagrophytes, var. interdigitalis* in 65 cases, *E. floccosum* in 60 cases and *C. albicans* in 8 cases. There were 4 cases in children below 9 years of age. Almost 90% of the patients were between 20 and 60 years of age. Only 19 patients were between the ages of 60 and 80. Dermatophytosis of the feet tends to recede as age advances.

There were 112 male patients and 94 female. The great majority were city patients. The 8 cases caused by *C. albicans* were of the hyperkeratotic clinical type.

Hall[21] found in the State of New York *M. gypseum* in a little over 50% of his cases, *T. rubrum* in over 38%, followed by *E. floccosum* and *C. albicans* in 6.5 and 5% respectively. *M. gypseum* also takes the first place in the statistics of Lewis,[22] Shapiro and Rothman[23] and Dolce and Nickerson.[24]

Phytids occurred in few of our cases. Vesicular and itchy eruptions of the hands were unusual, perhaps because these statistics are made up of patients of the manual workers group.

We wish to remark again, confirming the statement that dermatophytoses of the feet are not highly contagious, on the rarity of husband and wife coincidentally suffering from this condition. We also wish to call attention to the fact observed by us for many years, that barefoot patients do not suffer from superficial fungus infections of the feet.

Tinea of the glabrous skin. There were 78 patients with this condition. The etiologic agents were:

	Cases
M. canis	46
T. mentagrophytes	15
T. rubrum	5
M. gypseum	7
T. tonsurans	3
E. floccosum	2

More than half of these cases occurred in children below 9 years of age, only 12 cases were in adults; 8 patients also had tinea of the scalp.

Some of the lesions were highly inflammatory, pus producing manifestations of the kerion type,—one was due to *M. canis* and 5 to *T. mentagrophytes.* In one child 6 years old, the only lesion present was of the kerion type on his right knee. In these cases treatment with penicillin, as mentioned before, was successful in all.

Candidiasis. Of the 64 cases observed, 47 were located on and around the genital areas, 9 were of the mouth and lips and 1 was located in the submammary folds and axillas; one was a disseminate and systemic candidiasis with abdominal fistula,—a fatal case. The rest were of the hands and feet. In all cases *C. albicans* was the etiologic agent.

One of us (V.P.C.) has seen 3 cases in private practice of inverted psoriasis of the perigenital and submammary folds in women with secondary invasion by *C. albicans.* Roentgen ray treatment in fractional weekly doses, plus fungistatic and fungicidal treatment, was effective. The condition did not improve unless radiation was employed.

Parasitic sycosis of the beard and mustache.

The etiologic agent was predominantly *T. mentagrophytes* which was recovered in 32 of 41 cases; *T. rubrum* was isolated in 8 cases and *M. gypseum* in one case. Patients were usually below 50 years of age, only 3 were older patients. Both beard and mustache were affected in 10 cases, mustache alone in 16, and 15 of the patients presented lesions only on the bearded parts of the face. It is noteworthy that 33 of the 41 cases were in farmers or farm hands. All were white.

The lesions caused by *T. mentagrophytes* were usually highly inflammatory, as is true with many phytoses of animal origin. Many of these cases were of the purulent type with large boggy infiltrations, sometimes affecting the larger part of the beard and mustache. In these inflammatory cases with abundant secondary pyogenic infection, penicillin in aqueous solution injected locally and penicillin of the repository type intramuscularly, were the most effective treatment as was mentioned above.

Sycosis of the beard and mustache are seen but rarely in city patients.

Intertriginous dermatophytoses. These cases resembled clinically the lesions caused by *C. albicans.* The condition was erythematous and moist, sometimes oozing, highly inflammatory and even weeping. Eleven were examined mycologically; in 10 patients *E. floccosum* was recovered and *T. rubrum* in one. Most patients were young males, 7 of the 11 cases; only one was a woman. The location of the lesions was the inguinocrural regions in the men; in the woman, the lesions were also submammary. In some of the patients there was a long history of varied medication, much of it irritating. Secondary bacterial infection was always present, and several re-plants were necessary to obtain pure cultures of the dermatophytes. In the treatment of these cases demulcent, soothing and slightly antiseptic preparations were necessary before antimycotic measures could be put into effect. Pusey's liniment was the application of choice for the first 3 to 4 days.

Tinea nigra palmaris. Only 8 cases were seen. *C. wernecki* was recovered in every case; 4 were in males and 4 females, all white; 6 were city patients and 2 were rural patients. In 6 cases the right palm was affected and in 2 the left palm. All patients had a history of a fall or injury against the pavement or ground. The lesions presented the usual black areas of superficial desquamation and discoloration of the palm.

Local painting with tincture of iodine caused regression and final disappearance of the lesions in about 10 to 15 days.

Deep-Seated Mycoses

Chromoblastomycosis. This is the most common of the deep mycoses in our territory. Seventy-one cases were examined mycologically, but the total number of patients was much larger since many of them were seen only once and never returned for mycologic diagnosis and follow-up. In 70 cases *Fonsecaea (Hormodendrum) pedrosoi* was isolated and in one case *C. carrionii* (Fig. 4).

The patients were adults, from 20 to 90 years of age, except one case in a child aged 10 years. Of the 71 cases, 69 were in males and 2 in females; there were 64 whites and 7 colored. Sixty patients were residents of rural areas and only 3 of the city, but in all, the patients had some activity in contact with

FIG. 4

Chromoblastomycosis. Initial lesion.

wood. The location of the lesions was in the lower extremities in 35 cases; in the upper extremities in 33 and in 3 cases in the thoracic wall. In 3 instances affecting the upper extremities, the extension of the disease was upward through the lymphatic vessels, with the formation of granulomatous lesions along the course of these channels. This lymphangitic type occurred twice on the right arm and once on the left leg. Most patients report the original lesion at the site of an injury with a piece of lumber, the bark of a tree or the fronds or bark of sugar cane. In one case located on the knee, the patient was a climber of cocoanut-palms. Most cases clinically were of the verrucous type, a few of the tuberculoid and serpiginous types. Two of the 3 city patients were carpenters or woodworkers, and the other was an itinerant photographer.

In many patients the treatment of early lesions consists of surgical removal and later, in the more advanced cases, the combination of vitamin D_2 plus potassium iodide, first reported by Bonilla, gave excellent results.[25] In some cases with deep-seated lesions, involving extensive areas, ankylosis of one or more joints, atrophy of the muscles and deformities, made amputation imperative.

FIG. 5

Chromoblastomycosis. Unusual psoriasiform type.

In the culture of *C. carrionii* the greenish-black growth seemed a little more compact than that of *Fonsecaea (Hormodendrum) pedrosoi;* there were no reproductive organs of either the acrotheca, the hormodendrum or of the phialophora type. Cultures of this fungus were sent to Carrion of Puerto Rico and to Trejos of Costa Rica. The classification of this fungus as *C. carrionii* was suggested by Trejos, although this species is found more commonly in brain abscesses in man and mice. In all other cases *Fonsecaea (Hormodendrum) pedrosoi* was isolated in pure cultures (Fig. 5).

An important finding in one of our cultures was the presence of phialophora, hormodendrum and acrotheca types of sporulation in the same culture. This finding has been reported by several authors among them Almeyda,[26] Emmons, Hailey and Hailey,[27] Emmons and Carrion,[28] Pardo-Castello, Rio Leon and Trespalacios,[29] Azulay[30] and others. This may point to the unity of these species into one, with variable sporulation.

Sclerotia in the living tissue were seen several times growing into mycelia divided into chlamydospores. This phenomenon was reported by Calero[31] in 1946.

Sporotrichosis. All 10 cases were caused by *S. schenkii.* All were white patients, 9 were men and one a woman, and all were from rural areas. Their ages ranged from 15 to 75 years. The lesions were located on the upper extremities 9 times and one on the left leg. Of these patients, 8 had a definite history of injuries with vegetation. One had no recollection of any injury. A child with lesions on the right arm and axillary region had a history of an injury with a thorn of *Dichrostachys nutans, Benth.,* commonly known as "aroma," a nuisance bush common in all of Cuba.

The disease was of the lymphangitic type in all cases; no visceral, skeletal or disseminate types was encountered. The sporotrichotic chancre was present in all cases, some in a state of spontaneous regression.

S. schenkii was recovered in cultures in each case. Some cultures are white during the first 3 to 4 days, then become rapidly darker until a cholocate color develops, with a surrounding white halo which later disappears; other cultures turn dark in the first 48 hours.

Potassium iodide orally in doses of 3 to 6

Gm. daily was specific in all these cases. Sodium iodide intravenously was not as effective, but may be used when the patients are intolerant to iodides by mouth.

Actinomycosis. There were 7 cases of this mycosis. In 2 cases *A. bovis* was cultivated under anaerobic conditions. The other 5 cases yielded the typical yellow grains, but no cultures could be obtained under aerobic or anaerobic conditions in Petragnani, glucose broth and other media.

The youngest patient was 8 years old; 4 patients were between 21 and 30 years of age and the oldest was 50. Five were in males and 2 in females. Five were patients from rural areas and 2 were city dwellers. The location of the lesion was cervicofacial in 5 patients, one being bilateral distribution. Two patients had pleuropulmonary involvement, a child 8 years old and a man aged 50, and both had multiple thoracic fistulas.

In Petragnani's medium, under anaerobic conditions at 37° C., colonies appeared about the seventh day, soft, yellowish in color, of irregular surface; by about the twentieth day the colony was about 1 cm. in diameter. In agar-broth the colonies appeared about the seventh or eighth day, adherent to the walls of the test-tube in the form of yellowish spiderweb-like growth. Microcultures in glucose Sabouraud's media in one of our specimens showed bacteroid-like hyphae and in another colony there were many mycelial comma-like elements. Tinctorially they were gram-positive and nonacid alcohol-fast.

Emmons[32] suggests that under the actinomycoses should be grouped all mycoses caused by actinomyces, whether of the skin, the jaws, neck and face, the so-called Madura foot, actinomycotic meningitis, actinomycotic pleural and pulmonary infection and in other locations. Topley, Wilson and Begey, quoted by Emmons are of the same opinion. It seems reasonable to do this, but it should be by international agreement.

Emmons,[33] in 1938, isolated *A. bovis* from human tonsils in 37 of 200 pairs of tonsils removed at tonsillectomy. *A. bovis* also was obtained in cultures from carious teeth but repeated subcultures were required before classification was attained.

It is now admitted that *A. bovis* is a common saprophyte in human beings and in animals, especially of the mouth, becoming parasitic under yet undetermined conditions.

Mycetoma of the feet. There were 6 cases of this mycosis, all men between 21 and 50 years of age. Five were rural residents and one a city man. Four were colored and 2 were white. *N. brasiliensis* was isolated in 3 cases, *N. pelletieri* in 2 cases and *Monosporium apiospermum* in one case. The right foot was affected in five patients and the left foot in one (Fig. 6).

The rural patients were all of the laboring class, field workers or sugar cane cutters and loaders. All patients had a history of an injury days, weeks or months before the onset of local symptoms. The city patient from whose foot *Monosporium apiospermum* was recovered in cultures, was a shoemender. He had suffered an injury on the affected foot on dropping off a bus while in motion, 6 years before; it was the only injury the patient could remember. Lesions began a few months after this injury; he had never been to any rural area.

Monosporium apiospermum is the incomplete asexual, conidial form of *A. boydii.* It was recovered only once by one of us (F.T.); grains resembled those of the Nocardias, yellowish, with clubbed ends made up of chlamydospores. Cultures were visible on the third day, gray in color, with aerial mycelium. The surface of the medium was rapidly covered by the fast growing fungus; hypha were about 6 micra in diameter, branching in all directions, carrying sporophores with conidia on the free extremities. There were also lateral conidia, especially in older colonies. No ascospores were seen as described in *A. boydii.*

FIG. 6

Mycetoma. *N. brasiliensis.*

N. pelletieri grains were dark yellow with blunt ends. Colonies appeared on the sixth day after planting in Sabouraud's agar, aerobically; they were coral red in color, of slow growth and of soft, irregular surface. After several replants the red color faded and the colony became yellow, of irregular surface, honeycombed. Mycelium was bacteroid, gram-positive and nonacid alcohol-fast.

N. brasiliensis grains were yellow with club-shaped ends. Cultures in Sabouraud's grew at room temperature in 5 or 6 days. Colonies were hard and dry, pale pink to yellow in color. Growth was slow, about 1 cm. in diameter at the end of the twentieth day. In microcultures hyphae were less than a micron in size, many were dichotomous. Tinctorially they were gram-positive.

Carrion[34] has reported a case of mycetoma due to a *Cephalosporium* in Puerto Rico, and also a case of mycetoma caused by *Monosporium apiospermum* in the island of Santa Cruz in the lesser Antilles.[37]

An unusual case caused by *Madurella grisea* was reported by Neuhauser[36] of Chicago in 1955.

Rarer deep mycoses. Of the rarer mycoses, histoplasmosis has been reported twice in Cuba; once by Sanguily, Ferrer and Leon Blanco[37] with the lesion appearing on the tongue, and another by Barquet Chediak[38] in a child 6 years old with an ulcer of the foot and widespread subsequent invasion of the reticuloendothelial tissues; both cases ended in death. It is to be remarked that in a survey of the cutaneous sensitivity to histoplasmin, coccidioidin and tuberculin in Cubans, in 1952, by Pardo, Pardo-Castello and Tucker,[39] 20.5% were positive to histoplasmin, while only 2.1% were sensitive to coccidioidin, which the authors interpreted as specific sensitivity to histoplasmin and nonspecific positives to coccidioidin.

One case of cryptococcosis with multiple superficial, shallow ulcers of the skin in a patient with universal erythrodermia, probably a lymphoblastoma, has been under the care of Drs. F. R. Tiant, Pardo-Castello and F. Leon Blanco. *C. neoformans* was isolated from this case by Dr. Cesar Fuentes. The patient had been ill for about 10 years, but the cryptococcus complication dated probably from only a few months. This case will be reported fully in the near future.

One case of rhinosporidiosis was published by Dr. Leon Blanco[40] in a white girl, 10 years of age, who had a nasal polyp in which *R. seeberi* was found in the histopathologic sections. Cultures could not be obtained.

Summary

This is a report on 1,174 cases of superficial and deep mycoses as observed in Cuba.

The clinical as well as some mycologic aspects of these conditions are reported. The pertinent literature is amply reviewed.

Tinea of the scalp is most commonly caused by *M. canis.* One case is reported in a child one month old. The treatment of kerion with penicillin locally and systemically is considered most successful.

Most cases of onychomycoses are caused by *T. rubrum.* Treatment with 40% salicylic acid plaster followed by antifungal preparations is considered the best.

T. rubrum and *T. mentagrophytes* are the common agents in dermatophytosis of the feet, followed in order by *E. floccosum.*

Of the deep-seated mycoses, chromoblastomycosis was observed in 71 patients. In 70 *Fonsecaea (Hormodendrum) pedrosoi* was recovered in cultures. In one case the fungus was identified as *C. carrionii.*

Ten cases of sporotrichosis, 7 of actinomycosis and 6 of mycetoma of the foot are reported. From the mycetomas *N. brasiliensis* was recovered 3 times, *N. pelletieri* twice and *Monosporium apiospermum* once.

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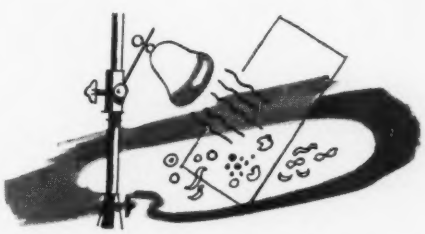

Infection in the Diabetic*

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DESPITE THE ADVENT OF INSULIN, newer technics in precise bacteriologic diagnosis, and the introduction of potent bacteriostatic and bactericidal drugs, it is a curious fact that the diabetic of today continues to develop infections more readily than the nondiabetic, the course of the infection is generally more complex, and therapy must be more vigorous and prolonged.

Exactly why this should be true remains a mystery. For many years it was a popular belief that the diabetic developed infection because elevated blood sugar levels were conducive to bacterial growth and proliferation. That this is true has been repeatedly questioned. It is known that the addition of glucose up to 1% to blood does not increase the rate of growth of staphylococci in culture media, nor does the addition of dextrose decrease the bactericidal activity of whole blood.[1] It has been shown, however, that while hyperglycemia alone does not facilitate bacterial growth, streptococci, pneumococci and *Hemophilus influenzae* grow much better on blood agar plates made with the blood from patients in diabetic acidosis and coma.[2]

If, as has been proposed, factors other than hyperglycemia predispose the diabetic to infection, the proof lacks conclusive evidence. One might reasonably assume that some fault in natural resistance (as reflected by a measurable immunologic defect) would explain this tendency; however, it has been demonstrated that gamma globulin levels in the well-controlled diabetic are essentially normal, suggesting that a failure of the immune mechanism is not a major factor.[3] This would imply, in part, that natural resistance and antibody formation are undisturbed, a finding somewhat at variance with the work of Richardson,[4] who demonstrated both impaired bactericidal activity of diabetic whole blood, as well as a decrease in antibody forming capacity. This work was further confirmed by Moen and Reimann,[5] who demonstrated the diabetic less capable of forming *acquired* antibodies than the normal individual. Richardson attempted to correlate the impaired bactericidal activity and decreased antibody forming capacity with the lowered resistance in diabetics. He found that antibody formation bore no relationship to the blood sugar level (using typhoid vaccine as antigen), although patients in poor clinical condition were somewhat less efficient in antibody production. He therefore decided to study the formation of antibodies to *B. typhosus* in rabbits under conditions of undernutrition and with hyperglycemia. He definitely demonstrated lower antibody titers in the malnourished group, but no change in the group made hyperglycemic. Since in all of his animals undernutrition was found to be associated with a striking decrease in liver glycogen, he suggested that the state of *cellular nutrition* is a significant factor in determining antibody response.[6]

Recent investigation of the properdin-system, considered by some to represent our most primitive defense mechanism against infection, has thus far shown no measurable defect of this system in diabetics.[7]

The demonstration that the whole blood of diabetic patients (regardless of sugar content) has weaker bactericidal power than normal blood led Cruickshank and Payne[8] to state that this loss of activity is related more to acidosis than to any other abnormality accompanying diabetes. While phagocytes of rabbits made diabetic with alloxan retain unimpaired the ability to engulf pneumococci, they lose some of their bactericidal power for these microorganisms. Dubos[9] has shown that lactic acid is highly bactericidal in acid reaction, while keto acids render bacterial cultures more resistant to acid reactions. Since keto acids accumulate *in vivo* in uncontrolled diabetes and starvation, it is suggested that these products might interfere with the natural bac-

*Read before the Section on Medicine, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

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tericidal effect of lactic acid, and that possibly the intracellular environment of the phagocytes reflects the metabolic disturbance of the body as a whole. In amplification of the possible role of lactic acid in combating infection, it has been shown[10] that the leukocytes of diabetics show an impaired glycolytic power which can be corrected back to normal by the addition of insulin. Conversely, treatment of normal leukocytes with cortisone produces a *decrease* in lactic acid production. Perhaps this defect in lactic acid production and the antagonistic effect of excess keto acids in uncontrolled diabetes holds a partial answer to the problem of infection in the diabetic. The applicability of this hypothesis to the human diabetic has yet to be proven however, and this presents a fertile field for more intensive study.

It has been proposed that protein malnutrition is a potent factor in rendering the diabetic more susceptible to infection. Certainly in his inability to utilize carbohydrate, the uncontrolled diabetic manifests a grossly inefficient mechanism for the utilization of all foodstuffs, and the descriptive term, "starvation amidst plenty" has sound basis in fact. It is striking that in all conditions in which protein catabolism is increased (e.g., tending to negative nitrogen balance) there is a drop in natural resistance to infections and toxins. This has been demonstrated in adrenalectomy, hypophysectomy and vitamin deficiency states by Marmorston-Gottesman and Perla.[11] It has been clearly demonstrated, however, that the diabetic is in negative nitrogen balance only during metabolic acidosis or when losing weight rapidly, and it is safe to conclude that while the decrease in resistance to infection in severe diabetes is in part a reflection of an increased protein catabolism, in the well-controlled diabetic, protein depletion plays an as yet unknown role in increased susceptibility to infection.

The role played by vitamin deficiencies has not been adequately investigated. The recognized response of certain diabetic neuropathic states to the administration of thiamine and vitamin B_{12} has been gratifying in certain instances, and the association of neuropathy (notably loss of sensation) with infection of the bladder, prostate, epididymis and lower extremity in diabetes has prompted several observers to suggest a cause and effect relationship. It would seem unlikely, however, that neuropathy, *per se*, contributes to infection except by decreased local tissue resistance, and by delaying subjective perception of a locus of inflammation. It is not uncommon to see diabetics with abscesses, cellulitis, or even gangrene, without significant awareness of the condition themselves. The recognized role of vitamins in cellular metabolism acting essentially as coenzyme systems suggests that in certain deficiency states (beriberi, pellagra, riboflavin deficiency, scurvy) infection might be more common, and such indeed is the case. On the other hand, however, in the well-controlled diabetic, studies thus far indicate no consistent pattern of specific vitamin deficiency. The recent interesting work concerning the role of pantothenic acid in the adrenal cortical synthesis of glucocorticoids (acting essentially as a coenzyme for acetylation) strongly suggests that the role of the B vitamins in diabetes needs reinvestigation.

Because the disturbance of fat metabolism has always played such a compelling role in the clinical and laboratory aspects of diabetes, a great deal of study and publicity has been devoted to this particular aspect. A number of years ago, Coates,[12] and Oppenheimer and Fishberg[13] demonstrated an increase in cholesterol deposited in the macrophages in the diabetic. The role of the macrophages of the reticuloendothelial system in combating acquired infections is of vital importance, and it is certainly conceivable that the rapidity with which infections progress in diabetics may be related to this abnormality. In addition to this lipid-infiltration of the macrophage system, several workers have shown that impaired fat metabolism is of even greater importance in relation to the readiness with which diabetics develop tuberculosis. It has been shown repeatedly that in the diseases in which resistance to tuberculosis is known to be decreased (diabetes, cirrhosis and chronic alcoholism) there is an abnormal fat metabolism.

There is a tendency in diabetes, because of the preferential utilization of fats, for the body to rapidly saponify neutral fats, with the resulting release of greater than normal quantities of glycerol. As early as 1927, glycerol was found to be the only alcohol capable of acting as the sole source of carbon for the growth of the tubercle bacillus, Long[14] and others hav-

ing noted a tenfold increase in the yield of tubercle bacilli by increasing the glycerol of the media. (Hence our current use of glycerol media for laboratory growth of the tubercle bacillus.) In simple obesity, where tuberculosis is actually less common, free glycerol can be readily esterified with the fatty acids into neutral fats which cannot be utilized by the tubercle bacilli. To test this hypothesis, Long gave rats already infected with tuberculosis glycerol intravenously and observed striking dissemination and a high yield of tubercle bacilli over normal controls. A less tangible but equally potent result of the disturbed fat metabolism is its contribution to the development of metabolic acidosis, depletion of fixed base, and resultant *tissue dehydration*. Dehydration alone has been shown to interfere with antibody release and cellular resistance, as demonstrated in adrenalectomized rats merely deprived of sodium chloride.[15] Administration of salt and water quickly reverses this.

The influence of the various endocrine disorders on the incidence and course of infection in the diabetic is of some theoretic importance here. Almost every hormonal substance of the body is directly or indirectly related to carbohydrate metabolism and the action of insulin. The recognized association of Cushing's syndrome, acromegaly, pheochromocytoma, and thyrotoxicosis with diabetes mellitus has demonstrated these metabolic interrelationships; however, infection seems to occupy no consistent place of correlation between these associated conditions.

Exacerbation and aggravation of certain infections following administration of adrenal steroids suggests that excess levels in diabetics might explain their tendency to infection, particularly tuberculosis. This is even more credible in view of the recognized amelioration of diabetes following hypophysectomy or adrenalectomy; however, it has been clearly shown that levels of plasma hydroxycorticoids are normal in the well-controlled diabetic.[16]

Perhaps one of the major etiologic factors in infection in the diabetic is vascular insufficiency. There can be no question that tissue anoxia as a result of poor blood supply contributes significantly to infections in the lower extremity. The impressive number of amputations in the diabetic following infection and gangrene attests to the importance of local tissue nutrition in maintaining the body's integrity against infection. It is recognized that the normal individual increases local blood supply in the presence of inflammation. The diabetic, on the other hand, responds to inflammation in regions of inadequate blood supply by actually developing vascular thrombosis and necrosis.

Specific Infections in the Diabetic

Skin infections. Infections of the skin in diabetes have given rise to a host of specific dermatologic terms which defy recollection as well as pronunciation. Greenwood[17] demonstrated that 25% of patients with diabetes give a history of cutaneous infection, and roughly 10% show active infection at any one time. Furunculosis occurs in 6.6% of diabetics, and 40% of diabetics show evidence of fungal infection of one sort or another, most commonly epidermophytosis. Studies of the skin[18] have shown that sugar in the skin closely parallels that of the blood, and that there is a significant amount of glucose in the sweat of the poorly controlled diabetic. For this reason it is worthwhile to note that, while the blood, skin and sweat sugar do not directly influence *bacterial* infections of the skin, there is good evidence to show that the growth of *fungal* infections seems to be *directly* related to this enriched medium. Monilia, mucormycosis, and a host of related systemic fungal infections have been reported in the diabetic with disturbing frequency.[19]

Gas-producing infections. The finding of gas in infected tissue spaces in the diabetic is a phenomenon which has been recognized for many years. We have come to believe, although with as yet scanty bacteriologic confirmation, that gas-producing organisms are active in a surprising number of infections which are seen in the diabetic. This capacity for gas formation is shown not only by the coliform group, but by staphylococci and streptococci as well. At one time, it was felt that crepitus in a gangrenous extremity was certain evidence of clostridial infection, and most vigorous amputative procedures were inaugurated. It is our current feeling that most, if not all of such infections are of streptococcal or coliform etiology and do not represent "gas gangrene," as such, nor is such radical surgery indicated. We have facetiously coined the phrase, "all that bubbles is not

clostridia." Our therapeutic approach to such problems will be outlined.

Tuberculosis in the diabetic. We have already alluded to the diabetic's predisposition to the development of tuberculosis. Early in the 19th century, Nicholas and Guedville[20] wrote of "la phthisurie sucree," while in England, Copland and Bradsley[21] stated that tuberculosis occurred so frequently in diabetes as to be a sign of the disease. That there is more than a casual relationship between the two is demonstrated by the fact that tuberculosis in the diabetic becomes clinically manifest and active at a period of life when the mortality peak from tuberculosis for the general population has declined.[22] It has been shown that experimental diabetes in dogs is associated with an increased susceptibility to the development of pulmonary tuberculosis.[23]

While the over-all mortality from tuberculosis has decreased remarkably in the past few years, tuberculosis is still three to five times more frequent in the diabetic than the nondiabetic,[24] and in children this figure is much higher. Pope[25] has shown in a study of a population of 140,000 children that tuberculosis is ten times as frequent among diabetic children, and Root[26] (prior to the advent of streptomycin) demonstrated that among adolescents, tuberculosis occurred sixteen times as frequently in the diabetic as in the nondiabetic. These are startling figures, and figures which we hope will change as the years bring us more effective means of regulating the juvenile diabetic.

Severity of the diabetes seems to influence the incidence of tuberculosis, since Joslin[27] demonstrated that 8% of diabetic patients within 3 years after recovery from diabetic coma developed tuberculosis. Histopathologic changes in the tuberculous diabetic are different from those in the tuberculous patient generally; in keeping with the accelerated course of the disease in diabetics, there is less to suggest the classically chronic nature of the disease, e.g., less pleural reaction, less fibrosis, and less residual bronchiectasis. Frequently the lesions are located at the hilus and base rather than peripherally (giving rise to the term of "Diabetic Tuberculosis").[28]

Prognosis prior to antimicrobial therapy was uniformly poor. Fitz[29] in 1930 showed that following the discovery of active pulmonary tuberculosis in a diabetic, 63% lived one year or less, 23% lived 1 to 3 years, less than 13% lived longer than 3 years and only 1 in 35 recovered.

Genitourinary tract infection. Aside from the disturbing increase in emergence of antibiotic resistant bacterial strains, perhaps the most challenging dilemma confronting thoughtful physicians today is the problem of chronic infection of the genitourinary tract. MacDonald and associates[30] have recently demonstrated an appalling incidence of infection of the genitourinary tract in a careful autopsy study. While it is difficult to demonstrate statistically an increase in genitourinary infection in the diabetic, there is no question in our minds of its increased incidence as opposed to the nondiabetic population. One might reasonably argue that, as a select group, the diabetic is more frequently catheterized than the nondiabetic, and this we feel is true. The hazards of the retention-catheter have recently been ingeniously pointed out by Kass.[31]

In a careful autopsy study of 195 patients with diabetes, Sharkey and Root[32] demonstrated the occurrence of purulent infection of the genitourinary tract in 35 patients, an incidence of 18 per cent. In this study, directed primarily at pyelonephritis, 70% of those infected showed sepsis with organisms of the staphylococcus and streptococcus groups arising from skin infections, subcutaneous abscesses, and lung, appendiceal, and ear abscesses, pointing up the significant role of hematogenous spread of infection in the diabetic.

Pyelonephritis, however, is not the only urinary tract infection of distressing proportions. Cystitis, prostatitis and epididymitis occur with alarming frequency, often with masked symptoms which make diagnosis difficult. We have learned the hazards of the forgotten Foley catheter, left in too long, of the forced prolonged bed rest, and of inadvertent dehydration. In addition, we, as others,[33] have come to regard infection of the genitourinary tract as a fugitive lurking in every diabetic, and now no longer wait for chills, fever, pain in the loin and prostration to herald an acute flare-up of pyelonephritis, but regard with caution any of our diabetics who complain of anorexia, nausea, constipation, headache, night sweats or backache, or who simply prove

difficult to control on a seemingly adequate program.

Besides infections of the skin and genitourinary tract, tuberculosis and fungal disease, it is worthwhile to observe that infections, such as osteomyelitis, endocarditis, infectious hepatitis, infections of teeth, middle ear, central nervous system, pancreas, and gallbladder all occur with greater frequency, more rapid spread, less striking response to therapy and with more associated complications in the diabetic than in the nondiabetic.

Case Presentations

The following 3 cases are presented to demonstrate the bizarre nature and gravity of certain infections in the diabetic, and the propensity for certain organisms to produce gas in the host tissues. Of greater significance, however, is the alarming failure on the part of the diabetic host to control and localize infection in the usual fashion.

Case 1. D. S. (No. 1364 JDH), a 31 year old Jewish male, was admitted with a 3 week history of sore, swollen gums and progressive swelling of the inside of the cheek with subsequent erosion and drainage of pus through lower lip. Fever was present for one week. Urinary sugar was 4+ and acetone 4+ on admission.

FIG. 1

(Case 1) This shows necrotic area of buccal mucosa with extension of infection through lower lip. Gangrenous stomatitis in a juvenile diabetic.

He had been diabetic for 24 years, requiring 50 units of insulin daily. There had been repeated kidney infections, and he had been totally blind for the past 2 years. Neuropathy, hypertension, and albuminuria were noted 5 years before. Four years prior to admission he had edema and exertional dyspnea which responded to digitalis and mercurial diuretics. The paternal grandfather died of diabetes.

Examination revealed a diffuse, tender, warm swelling of the entire right side of face and mouth, erosion of a lesion through the lower lip and drainage of foul smelling material. A grey pseudomembrane covered the buccal mucosa (Fig. 1).

Cultures showed a gram negative rod and anaerobic streptococci, no fusiform bacilli were seen. The chemical acidosis was readily controlled with 100 units regular insulin and fluids.

The patient expired suddenly on the 4th hospital day, in the face of apparent improvement in the general status and condition of mouth. Autopsy was not obtained. Death was thought due to myocardial failure. Blood cultures were sterile.

Case 2. G. M. C. (No. 30624 JDH), a 45 year old Negress, was in good health until 2 weeks prior to admission. She was admitted with infection and gangrene of the right foot, progressing over a 2 week period. Beginning as callus at the base of great toe, infection spread rapidly despite elevation, bed rest, warm compresses, sulfonamides and penicillin.

FIG. 2

(Case 2) Multiple collections of gas bubbles are seen in the soft tissues of the foot of a diabetic with gangrene.

FIG. 3

(Case 3) A large collection of gas, both in small bubbles and one large collection are seen beneath the left diaphragm. The left kidney is clearly outlined.

No previous history of diabetes was admitted. Polyuria and polydypsia had been present for 5 or 6 years. Anorexia and mild discomfort in the leg and foot were the only symptoms. The urinary sugar on admission was 3+ and acetone 1+. X-ray examination of the foot is shown in figure 2.

Following control of the acidosis, the wound was debrided, at which time copious foul smelling material bubbled out of the wound, from which a heavy growth of *Staphylococcus aureus* was cultured. Antibiotic therapy consisted of penicillin and streptomycin. Following subsidence of the acute process, patient underwent uneventful below-knee amputation. Her newly discovered diabetes was subsequently controlled in 15 units of insulin daily.

Case 3. A 47 year old Italian housewife was admitted to a local hospital on Jan. 2, 1957, because of pain in the left flank and a temperature up to 103°. X-ray studies at this time showed pockets of air outlining the left kidney (Fig. 3), but because the symptoms and fever rapidly subsided on penicillin and tetracyline, she was dismissed and followed as an outpatient. Her diabetes, previously controlled on 30 units of insulin, improved over the next month, so no insulin was required, presumably due to progressive loss of weight. During this period, aside from anorexia and mild flank pain, she did reasonably well. There were no bowel or urinary symptoms, and no fever.

On Feb. 10, 6 weeks later, she developed sudden sharp pain in the left chest, followed by cough which produced blood and a brownish foul smelling material (Fig. 4, A and B). She was admitted to another hospital where thick bubbling purulent material was aspirated from the left flank, from which *Proteus vulgaris* was cultured.

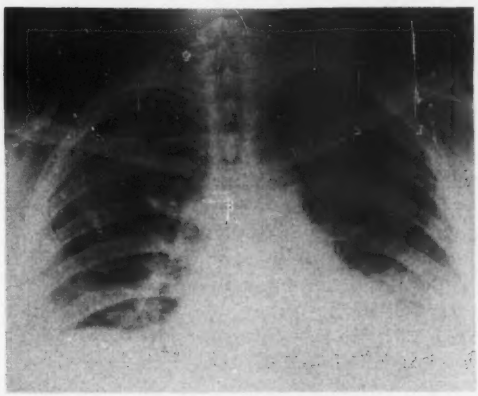
Surgical exploration of the left kidney area revealed an extensive abscess cavity in communication with the left chest by way of a small necrotic area in the left diaphragm. Her course thereafter was one of progressive decline with shock, bilateral pneumonia, and cyanosis. Cultures from the abscess cavity, sputum, urine, and blood all grew out *Proteus vulgaris.* Antibiotic therapy included streptomycin, chloramphenicol, novobiocin, and neomycin. At no time was she in diabetic acidosis.

Autopsy revealed rupture of a small diverticulum of the descending colon in communication with the left retroperitoneal area and left thoracic cavity with a patent bronchopleural fistula. Extensive bilateral Proteus pneumonia was also present.

Suggestions for Treatment of Infections in the Diabetic

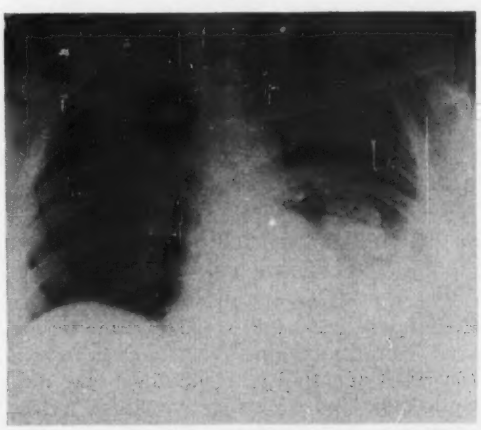
1. Precise localization of site of infection.

FIG. 4, A



(Case 3) This shows the chest at onset of flank pain. Haziness at the left base; no pulmonary symptoms are present.

FIG. 4, B



(Case 3) Appearance of the chest 6 weeks later at the onset of chest pain and hemoptysis. There is density at left base, and involvement of left perihilar area.

2. Adequate debridement or drainage.
3. Judicious local measures.
4. Accurate bacteriologic diagnosis.
5. Antibacterial sensitivity studies.
6. Comprehensive antibacterial therapy.
7. Supportive measures.

Since we believe the diabetic with infection does not always behave as the normal individual with a bacterial infection, we advocate that a most diligent search be made for smouldering infections in any uncontrolled diabetic in whom the cause for the difficulty is not readily apparent. This includes particular attention to teeth, gums, heart, accessory nasal sinuses, ears, prostate, kidney, epididymis, skeletal system, skin and perirectal tissues. Fortunately, gallbladder, pancreatic and pulmonary infections usually announce themselves.

We cannot emphasize too strongly our belief that surgical drainage at the earliest possible moment saves lives. Our natural tendency in the antibiotic era is to temporize with lesions which 15 years ago would have been drained without hesitation. It is likely in the second case presented here that the injudicious use of hot compresses contributed to the rapid development of gangrene. Local measures of cleanliness, elevation, and avoidance of trauma to the lower extremities do more to aid in localization of infection than do any other steps, and in all cases where blood supply to a part is marginal, heat is to be avoided. We have been impressed by the beneficial effect of hypothermia and freezing of gangrenous extremities. Once the decision to remove a diseased extremity is made and a line of demarcation is established, we advocate the use of ice-immersion of the affected part prior to operation, particularly if any delay is anticipated. We have kept legs and feet on ice for several days when a precarious situation has demanded that operation be delayed, and have observed a rapid decrease in manifestations of general toxicity, and a rapid disappearance of pain and discomfort.

The significance of adequate bacteriologic study is self-evident. Despite this, seldom are good cultures obtained of materials which may subsequently yield the organism of a septicemia. Under such circumstances a clear knowledge of the organism and its antibiotic antagonists is *vital.* It is difficult to make generalizations concerning appropriate antibiotic therapy, but the application of certain basic pharmacologic facts will make treatment more effective. In the diabetic, where infections often progress rapidly, immediate attention should be given to even the simplest appearing lesion and every effort should be made to determine the specific etiologic agent. Therapy should be as specific and intense as possible, and aimed at attaining bactericidal concentrations of the antibacterial agent at the site of infection as rapidly as possible. In the more serious infections this usually means the parenteral administration of a bactericidal drug, such as soluble forms of penicillin, streptomycin, bacitracin, neomycin, or polymyxin. If bacteriostatic drugs such as the tetracyclines, chloromycetin, erythromycin, or novobiocin are utilized, they should be given intravenously initially. In many of the deep or chronic infections, treatment with some suppressive agent, such as the sulfonamides, should be maintained for 4 to 6 weeks. This is particularly true in deep abscesses, osteomyelitis, and chronic pyelonephritis. When adequate kidney function is present and fluid intake approaches normal, we have not hesitated to employ drugs hitherto considered nephrotoxic (neomycin, bacitracin and polymyxin). Good diabetic control usually follows in close temporal relationship the control of the infection.

These principles set forth, the cases presented and this discussion of some of the factors in the decreased natural resistance of the diabetic host to infection, have been pointed out to emphasize certain aspects of a subject which still pleads for further study and investigation. Perhaps each one of us who sees diabetics could inaugurate a project to study the effect of certain therapeutic or prophylactic measures on their diabetic populations, from which some light might be cast on this complex problem of infection in the diabetic.

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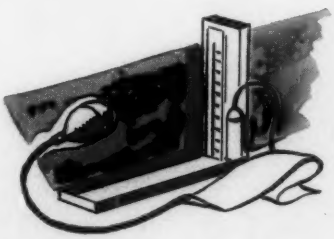

Use of Muscle Pedicle Cancellous Bone Grafts*

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The author describes his experiments and clinical application of muscle pedicle bone grafts, which have the advantage of supplying a viable structure in the surgical attack on certain fractures and in certain orthopedic procedures.

THE FIRST USE OF VIABLE bone grafts dates to the work of Phelps.[1] Writing in 1891, he described a method of transplanting viable bone to repair the loss of substance in the tibia. It consisted of approximating the tibia of a living dog to the tibia of a boy, then incorporating the extremities of both boy and dog in one external appliance. This procedure failed to achieve maintenance of the blood supply of the graft for reasons that are now obvious. Phelps' principle was later used more successfully by Curtis[2] and others when they introduced ipsilateral transplantation of the fibula into the tibia.

Utilization of grafts attached to tendons is credited to Hibbs.[3] In 1911, he transplanted the patella in this way for arthrodesis of the knee. And in 1926, he similarly transferred the trochanter of the femur for fusion of the hip.[4]

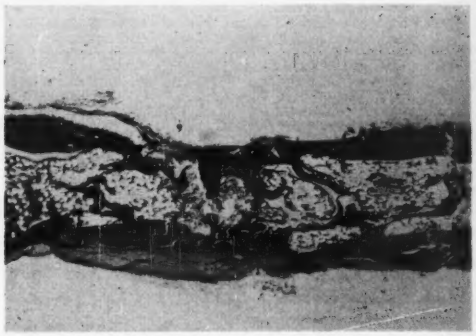
Muscle pedicle bone grafts for repair of cranial defects were described by Watson Jones[5] in 1933. Cole[6] used them in 1940 for treatment of nonunion of the mandible.

Hellstadius,[7] in 1942, reported a series of experiments on rabbits in which he transplanted cortical bone with and without tendon pedicles. It was his conclusion that a tendon pedicle did not contribute to the viability of a bone graft.

Experiments with Muscle Pedicle Cancellous Bone Grafts

In 1952, Taylor and I,[8] working with dogs, transplanted grafts consisting of cancellous bone from the iliac crest and pedicles from the fascia femoris muscles. All these grafts remained viable. The experimental work

FIG. 1

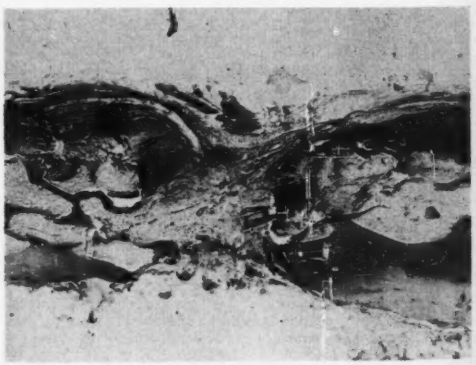


Specimen of iliac crest 6 weeks postoperatively. Fracture line is healed and bone is viable. Blood supply is maintained through a muscle belly pedicle.

which Hartley and Silver[9] did on rabbits substantiated and advanced our observation that cancellous bone will maintain its viability when separated from its host, provided it is attached to muscle fibers.

To determine if the muscle pedicle main-

FIG. 2



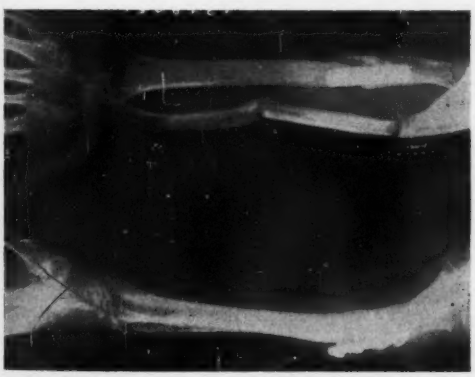
Specimen of free cancellous iliac bone fractured 6 weeks previously. Note fibrous substitution of the fracture and avascular necrotic bone.

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

tains enough blood supply to aid in healing a fracture in such a graft, I conducted another series of experiments on dogs. On one side of each animal a graft cut from the iliac crest was left attached to the fibers of the tensor fascia femoris muscle and transferred to soft tissue away from the donor area. On the opposite side a graft, also cut from the iliac crest but without a muscle pedicle, was similarly transferred to soft tissue away from the donor area. Both grafts were incompletely sectioned with an oscillating saw. At weekly intervals one of the animals was sacrificed and the areas of the grafts were examined. In each animal it was observed that the saw-cut in the muscle fiber pedicle graft had healed promptly (Fig. 1). But the saw-cut in the graft without blood supply had failed to heal, and the familiar fibrotic invasion and creeping substitution had ensued (Fig. 2). It was therefore concluded that a muscle belly pedicle furnishes sufficient blood supply to heal a fracture made by a saw-cut.

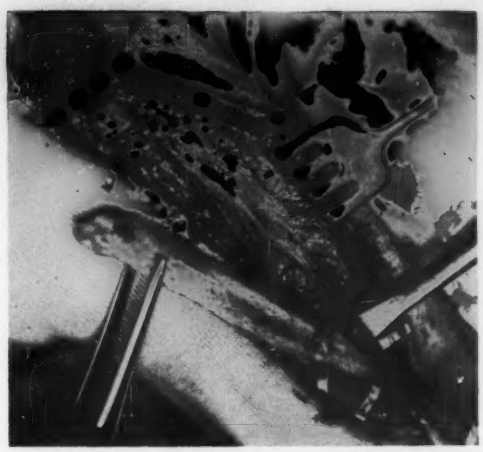
The next question I sought to answer was whether or not viability can be maintained when a cancellous bone graft is transplanted from one muscle belly to another. At the time I was trying to resolve this question, I was consulted by a man with an ununited ulna of long standing (Fig. 3). The usefulness of his hand was greatly diminished as a result of the concomitant fibrosis and impairment of the vascular and nerve supplies. He had had many types of treatment, the last of which was a fibular transfer. When I explained that a muscle fiber pedicle cancellous bone graft might give him a stable and functioning arm, he agreed to let me attempt a two stage substitution procedure.

FIG. 3



Anteroposterior and lateral roentgenographic views of a fibular transfer to the ulnar defect which has not united at the proximal end of substitution.

FIG. 4



Dissected ulna. The fibular substitution is partially united at the distal end of the graft.

FIG. 5

Bone graft prepared from the iliac crest and left attached to a pedicle of intact lateral muscles. The intramedullary wire extends throughout the length of the graft.

FIG. 6

This photograph was taken 4 weeks after the forearm was sutured to the iliac crest.

The ulna was exposed through a longitudinal incision in the area of the unsuccessful fibular transfer, and the avascular ulnar fragment was removed (Fig. 4). The iliac crest on the same side was exposed. A full section of iliac crest was then turned outward, leaving portions of the gluteus medius and tensor fascia femoris muscles attached (Fig. 5). A longitudinal hole was drilled in the cancellous bone graft and in each of the two ulnar fragments for the acceptance of a small Steinman pin. The arm was brought to the pelvis, after which the inner skin surfaces of both the pelvic and the arm incisions were united. The prepared muscle pedicle bone graft was then placed over the ulnar defect. The Steinman pin was passed through the proximal fragment of the ulna, the bone graft, and the distal fragment of the ulna. When this was completed, the skin was closed medially over the grafted ulna. Application of a plaster cast, incorporating the body, arm, and thigh, completed the operation.

The cast was removed at the end of 4 weeks and the skin incision, uniting the forearm and the pelvis, was reopened. It was noted that the graft was still securely held by the intramedullary rod (Fig. 6). The muscles of the forearm had become attached to the graft. When the forearm was detached from the pelvic muscle pedicle, blood flowed vigorously from the graft. The origin of this blood was the muscle bodies of the forearm. It was concluded, therefore, that cancellous bone remains viable when transferred from one muscle belly to another (Fig. 7).

The wound in the forearm was sutured. It healed by primary intention (Fig. 8). Because the gross malformation had persisted, and because the ulna had not united at the

FIG. 7

Section from the muscle pedicle bone graft. Note areas of viable bone and fibrous reactive marrow spaces.

FIG. 8

Closed forearm wound.

FIG. 9

Section of cancellous bone graft obtained when arm was amputated. Note maintenance of viability.

distal end of the graft, the arm was amputated. Inspection of the graft at this time showed that it was still viable (Fig. 9).

FIG. 10

Roentgenogram of interarticular fusion done for degenerative arthritis. Note screws maintaining graft and the healed osteotomy.

FIG. 11

Acromion process attached to a pedicle of deltoid muscle.

Clinical Application of Muscle Pedicle Cancellous Bone Grafts

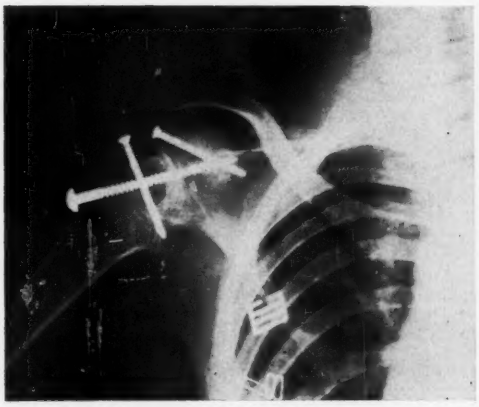
I first used the muscle pedicle cancellous bone graft in hip fusion.[10] The essential features of the procedure were: (1) preparation of the graft from the anterior iliac crest and the pedicle from the tensor fascia femoris muscle; (2) transfer of the graft to the hip joint; (3) interarticular arthrodesis; and (4) intertrochanteric osteotomy (Fig. 10).

Subsequently I successfully used muscle pedicle cancellous bone grafts in other ortho-

FIG. 12

The glenoid and humerus have been denuded of cartilage and secured with a wood screw. The pedicle graft placed across the denuded joint is secured with 2 screws.

FIG. 13



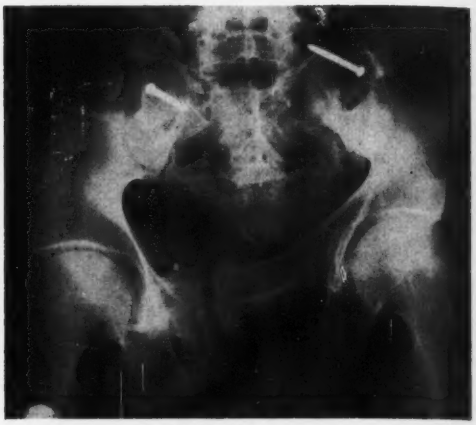
Roentgenogram of shoulder fusion carried out for flaccid paralysis of the upper extremity.

pedic procedures. These are briefly described in the following paragraphs.

Arthrodesis of the shoulder joint. The shoulder is approached through an incision made across the acromium process and extended anteriorly onto the deltoid muscle. The graft is prepared from the entire acromion, and its pedicle is prepared from the deltoid muscle (Fig. 11). Exposure of the shoulder joint is accomplished by removal of the rotator cuff and capsule. The glenoid and humerus are denuded of their articulating cartilage and held in contact by a wood screw extending from the humerus into the scapula. The roughened graft is then placed across the shoulder joint and secured by two bone screws (Fig. 12). Figure 13 shows this method of arthrodesis carried out for flaccid paralysis of the shoulder.

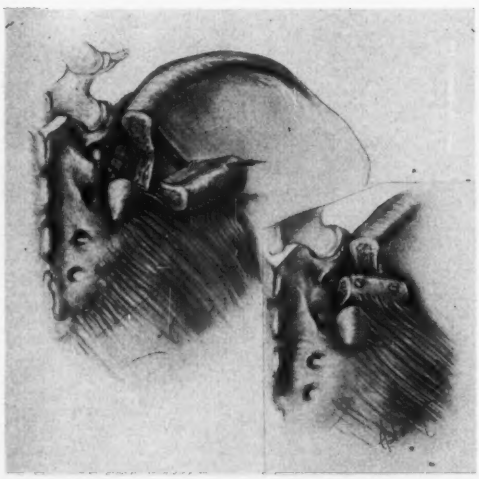
Sacro-iliac fusion. The sacro-iliac joint is approached through either a Campbell[11] or a Smith-Petersen[12] operation. It is then bridged by a graft cut from the posterior crest of the

FIG. 15



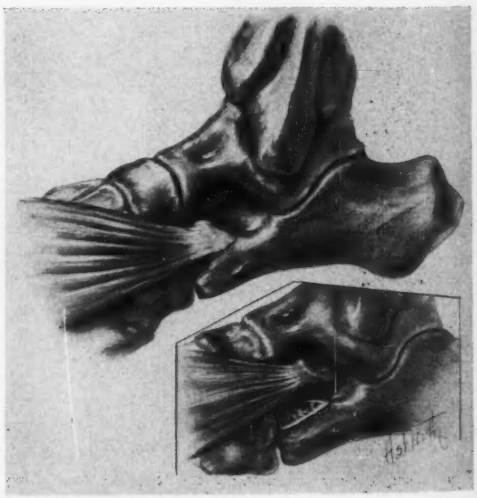
Roentgenogram of bilateral fusions of the sacro-iliac joints done for post-traumatic pain. Fixation on either side is maintained with 1 screw.

FIG. 14



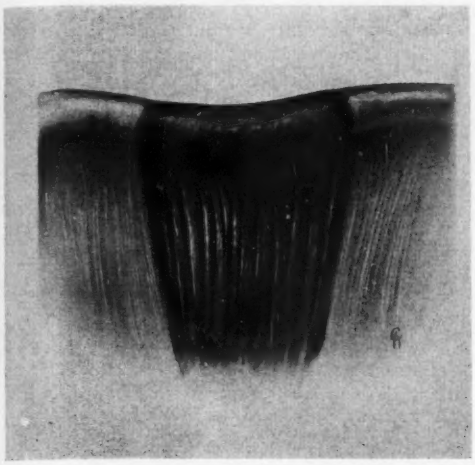
Schematic representation of pedicle bone graft prepared from the gluteus medius and maximus muscles. Fixation over the sacro-iliac joint is maintained with 2 screws.

FIG. 16



Method of transferring the anterior tubercle of the calcaneus to the sinus tarsus in triple arthrodesis.

FIG. 17



Schematic representation of a pedicle graft in the presence of infection. Note central area of viable muscle and bone.

ilium with an attached pedicle from a portion of the gluteus maximus muscle. Fixation of the graft is maintained by screws (Figs. 14 and 15).

Triple arthrodesis. A portion of the os calcis is detached with the short toe extensor muscle. A standard intra-articular triple arthrodesis is done, after which the fragment is attached in the area of the denuded tarsal sinus (Fig. 16).

Lumbosacral fusion. Adaptation of the muscle pedicle cancellous bone graft to fusion of the lumbosacral joint was not successful in my hands. I did a total of 20 lumbosacral fusions by this method. The graft was cut from the posterior crest of the ilium and the pedicle was taken from the sacrospinalis muscle. The graft and its pedicle were then transferred to the lumbosacral area. Much difficulty was encountered in avoiding tension on the blood supply of the pedicle. When tension could not be avoided, the blood supply to a portion of the pedicle was lost. The operative sites in 2 patients became infected, and sequestrations were necessary. Nevertheless, in the areas in which the pedicle was viable the graft remained alive, despite the infection (Fig. 17).

Conclusions

From experimental studies and clinical experience, it is concluded:

1. A cancellous bone graft remains viable when attached to a pedicle derived from muscle fibers.

2. The blood supply from such a pedicle is sufficient to maintain viability and to produce healing of a fracture in the graft.

3. A cancellous bone graft retains viability in the presence of sepsis when it is attached to a viable pedicle.

4. Cancellous bone transferred from one muscle belly to another remains viable.

5. Muscle fiber pedicle cancellous bone grafts can be used successfully in selected orthopedic procedures, such as arthrodesis of the hip, shoulder, sacro-iliac, and posterior tarsal joints.

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A Project for the Creation of Better Understanding of Psychiatry by the General Practitioner*

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For a number of reasons it is impossible for every patient, who has difficulties which fall into the field of psychiatry, to be seen in consultation or be treated by a psychiatrist. The family physician is the one ideally suited to manage many of the psychiatric problems which trouble his patients.

PSYCHIATRISTS have, traditionally, kept pretty much to themselves. In the past they have practiced mostly in institutions with which other physicians had very little connection. They developed a language of their own which no one else understood, sometimes including themselves. They usually sought their specialty training where other specialists were not found. They managed the kind of patients no one else wanted. They published their own journals which other physicians seldom read, or even saw. They have inadequately communicated their findings about patients referred to them by other physicians. In general, they have rather thoroughly isolated themselves from the rest of the medical profession, and apparently with the blessing of the other doctors. Since World War II, however, psychiatry has not only become more respectable but, in some circles, is even fashionable. Different people have come into the specialty; they have taken a wider interest in the more commonplace problems of people. Now, psychiatrists in large numbers are working in clinics, general hospitals, and in private practice alongside other physicians. There still remain, however, certain obstacles to communication between the two groups. Sensing this as an important problem, a group of general practitioners approached the American Psychiatric Association a year and a half ago proposing a joint attack on the problem. As a result of these preliminary talks, the American Academy of General Practice and the A.P.A. each appointed a committee to work as a liaison agency to formulate a method by which psychiatric knowledge could be made continuously available to other branches of medicine. Their efforts resulted in obtaining a grant of money from the Lasker Foundation which made it possible to set up a project in the Central Office of the A.P.A. This was called the General Practitioner Education Project, and has been in official operation since last April.

The immediate objectives of this project are to study and develop practical methods by which postgraduate training in psychiatric principles can be made available to the general practitioners. Various types of courses, educational media, and written material are being investigated and tried out. The hope is to find the most practical means of getting across the most information to the greatest number of physicians.

That this project is timely and important needs no justification. Obviously, we could all be better physicians if we were equipped to handle a greater variety of problems that come our way. There is no question but that psychiatric problems represent a large part of the case load of any physician. Handling them with understanding can increase the physician's usefulness to his patients, and the satisfactions he will get from his work.

From a psychiatrist's knowledge of the nature of human beings, and, in particular, the nature of neuroses and psychoses, certain estimates can be made of how far and how expertly a family physician can go in han-

*Read before the Section on Neurology and Psychiatry, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

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dling psychiatric problems. I will attempt to approach this from two points of view: (1) what can the family physician legitimately handle if his training and experience has *not* included any special emphasis on psychiatry; and (2) within the limitations of time, etc. which beset the family physician, how far could he go if he were to advance his psychiatric knowledge to a moderate degree? Furthermore, I will try to define some of the practical obstacles which might stand in the way of the family physician doing as much as the experienced psychiatrist does.

In the first place, the family physician's role in the life of his patients fits him for doing something more than what we might call "first aid psychiatry." Furthermore, his medical background equips him to do a job which is qualitatively more profound and valuable than can be done by a psychologist or social worker who may actually have a greater technical knowledge of psychiatry. Still further, the family physician is very often in a position in which he can do more good in certain psychiatric problems than an experienced psychiatrist. In other words, it is *not* valid to assume that the general practitioner's role in mental health is merely that of a "junior" or "assistant" psychiatrist who is equipped to handle only minor psychiatric problems. Instead, the family physician can, and must fill a role in the field of mental health for which no other professional person could ever qualify, even though the latter might have greater experience in the field. In the same way, parents can do certain parts of the job of educating their children which even the most expert teacher could never accomplish, except with her own children. This example might be carried over to an accurate analogy by stating that the family physician's role in the mental health of his patients comes very close to that of a parent, while the psychiatrist's role is more likely to be similar to that of a teacher.

The family physician enjoys a position and a responsibility which is an extraordinarily unique one, and one which will represent his greatest single asset when it comes to approaching problems of mental health. This position is made up, in part, of the following qualities: (1) Behind him lie centuries' old traditions of medicine's interest in the sorrows and tribulations of mankind. These traditions serve to bring people to their physicians when they are in trouble, regardless of the nature of the trouble. The only other profession with a similar tradition is the clergy. (2) Secondly, medicine as a profession, and each physician in his training is imbued with a deep sense of responsibility for the life-or-death decisions which must be made in the practice of medicine. No other group of people have such training, or such a sense of responsibility, to guide them. (3) The individual physician shares the tradition of medicine in the objectivity with which he approaches each individual. This objectivity, which takes no partisan stand on racial, religious, social, economic or moral questions is one of the most important foundations for building up skill in the handling of psychiatric problems. The physician is interested in only two things insofar as his patient is concerned,—that of preserving his health and contributing to his happiness. He hopes, of course, to get paid for his services, but that is generally taken care of if he does his best on the other two items. The patient is aware of this tradition of objectivity, and this awareness will be responsible for many persons seeking help from their physician, rather than from other sources where they can anticipate a predetermined judgment. (4) The physician, more than any other professional person, is trained to see his patients as individuals rather than as statistics. The concept of "individual variation" and the rarity of the "classical case" have been pounded into him by his professors and his own experience so much that he is not as likely as others are to arrive at the false generalizations which are responsible for most of the mistakes in sociologic theories. Seeing the patient as a product primarily of his own life's experiences is the essence of clinical judgment in all branches of medicine, and especially in psychiatry.

These qualities, interest, responsibility, objectivity and individualized judgment are the assets of medical training which equip the family physician to handle a large share of his patient's emotional problems. They are known to the public through the reputation which American medicine has developed. They are responsible for the fact that patients come to their physicians expecting to get, not only sympathy, but, above all, the truth based on wisdom and an objectively

considered judgment and a deep interest in individual human welfare. They represent the practical ideals of medicine, and if we do not make the most of them, it will be a personal failure on our part, and not a reflection on the ideals themselves.

In order to appreciate how these "medical assets" might be put to use in helping patients with their emotional problems, it will be necessary for us to outline what the nature of these problems are likely to be. We psychiatrists have been most remiss, heretofore, in expressing in simple terms the commonplace facts about the neurotic or psychotic person. Let us try to outline these facts briefly. What we first notice about this patient, regardless of whether we diagnose him as neurotic or psychotic, is that he is unhappy and in trouble. His complaints tell us nothing more than this, they do not tell us what the trouble is or how it evolved, but only that he is in distress. As we get to know the patient better, which means, what kind of a life does he lead—what does he do with his time—what are and have been his experiences, we begin to see the other most outstanding characteristic of this kind of person; that is, his particular way of handling his responsibilities. We will notice that throughout life he has been, in some way and to some degree, avoiding responsibility. He will not tell us that, but we can guess it from the way in which he tries to blame others for all his failures, and from the way in which he consistently makes excuses for not trying anything which carries with it responsibility. As we fit the pieces of information about him together, we see that his unhappiness is the predictable end-result of a lifetime of trying to avoid responsibility. Let us not be deceived by the evidence he submits to disprove this. The fact that he does have responsibilities and that he even manages to take care of them, and sometimes does a fairly good job at it, does not negate the fact that he also tries to avoid them. He does not always succeed in avoiding them, but he tries. What he does in attempting to avoid them is most likely what gets him into trouble. The neurotic and the psychotic differ from each other primarily in the lengths to which they go to avoid responsibility. The neurotic takes his responsibilities, but reluctantly, complainingly, and expects an excessive reward for having done so. The psychotic stops at nothing to avoid responsibility, and that is what makes him appear "crazy" to others, since this is the very essence of irrationality.

Taking these two sets of characteristics into account, we can now illustrate what the family physician can do for the mental health of his patients. In the first place the physician can, and does set an example for his patients in the same way that the parent sets an example, whether good or bad, and thus has a decisive influence on the child's development. The example set by the physician is through his general professional and social conduct in his community, and specifically in the way in which he treats the patient in question. His patience, his interest, his objective judgment, his concern for *what* people *do* rather than *who* they *are*,—these are the very qualities which we want to instill in the patient. We can teach them, as the parent does, by practicing them ourselves. If, on the other hand, we consider the patient's complaints as our only concern, and give him some kind of pill to make him more comfortable, we are fostering his own irresponsible way of living, which is designed to do the same old things in the same old way but in the hope each time of coming out of the experience feeling more comfortable about it.

Beside the simple but all-important function of setting a more reasonable, more responsible, more interested example for the patient, the physician can do something else of great value. This, again, is something the parent can do for a child, and that is to give the patient the benefit of his own life experiences. As a physician you may not find a ready answer to some dilemma a patient appears to be in at the moment, but you might see that it is not the type of thing which happens in your own life. The absence of such dilemmas in your life may have something to do with the fact that you are busy using your time working, playing golf part of the time, and socializing with friends. You could help the patient by encouraging him to use more of his time in work, hobbies and friendships, and more often than not there will not be any time left over for him to get into the troubles which always seem to beset him. This illustration highlights the extent to which a physician untrained in psychiatry can go in helping his emotionally

troubled patients,—given the time and interest; he can teach the patient what he has learned himself about how to live a successful and satisfying life. He does not need to know too much about the patient to do this. He only needs to get the patient's cooperation in trying something different in his own life.

If in addition to being trained in the science and art of physical medicine, the physician also takes advantage of opportunities which come to him to advance his knowledge in the more technical side of psychiatry, he can do more than the above. Learning more about psychiatry consists primarily of acquiring a greater understanding of peoples' ways of thinking, particularly those distorted ways of thinking which we see in the neurotic and the psychotic. Psychiatry is not, as you might suppose, a study of specific diseases, their causes and their cures, but rather a study of rationality and irrationality. The medium through which this study takes place can be only that of human relationship. If you were to undertake such an educational program for your own advancement, you would not necessarily become more successful in handling psychiatric problems, but you would be likely to find ways of handling them more efficiently, more quickly and with greater confidence. Your limitations would probably be the same as we mentioned before, and that is you could help your patients to the extent to which you, yourself, have mastered the art of living happily and productively.

Discussion (Abstract)

Dr. I. Phillips Frohman, Washington, D. C. It is impossible for Dr. Goshen to convey in 20 minutes how many man-hours have been spent by him and by all of us on the liaison committee of the American Psychiatric Association and the American Academy of General Practice in developing the project he mentioned.

Through no fault of psychiatrists it has taken psychiatry many, many years to arrive at the proper level of respect and understanding by physicians and nonphysicians alike.

We general physicians, without considering the word "psychiatry" in our daily vocabulary with patients, have been practicing a mild but very efficient form of psychiatry since the beginning of medicine as such. Lately our form of psychiatry has been termed "psychosomatic medicine." We general physicians develop our own individual "brand" of psychosomatic approach to our patients. It is difficult and almost impossible for a physician in the northern part of the country to use the same approach as our southern colleagues. Likewise the approach to, and reasoning with our "nervous" patients, our "upset," and "confused" patients must be a bit different in a small town practice than in a large city practice. The reasons I believe are obvious. The environment, the recreational facilities, and the closeness of the population in the small town, as compared with the city, are but a few of the factors. Our results are the same I am sure. Most of these patients do not have to be referred to the psychiatrist.

Normal and well adjusted physicians have the same "normal" conflicts as their patients do. These conflicts and problems arise in their homes, their children, their office help and, more important, their patients. Perhaps our education and work has enabled us to view these conflicts more objectively and thus we can extricate ourselves more readily than our patients. And as Dr. Goshen mentioned, "our own conflicts are our own teachers." Our patients are not so fortunate and they come to us for help. Shall it be in the form of tranquilizers, barbiturates and other drugs,—and only these? Or shall it be in discussion of, or, better still, listening to their conflicts?

Dr. Goshen mentioned that we physicians set an example in the community and to our patients. Patients complain that physicians insist that they discontinue smoking for various reasons, yet in the same breath the physician behind the desk blows smoke into the patient's nostrils. And we try to diminish the corpulence of our patients, yet we show the "chubbiness" of our excellent appetites and food excesses. This is not good psychiatry.

These are minor problems I bring to your attention. I believe that we general physicians in this turbulent age of the jet and "sputnik" are ready for more advanced knowledge in the field of psychiatry so that we may better understand our patients' deeper and more acute troublesome problems, and thus help them with reasonable judgment and accuracy.

The reason for the project discussed is for a closer association and relationship with psychiatrists throughout this country. More psychiatry must be taught the students, interns, and residents. That is not too great a problem for the medical schools. The important job is to teach the practicing physician. How are the psychiatrists to get the educational material to us? In the development of this G.P. project, there is under consideration the association between sections of the state medical society, the state chapters of the American Academy of General Practice, and the state branches of the American Psychiatric Association. Under consideration is the suggestion that there might, and very well should be an increased amount of postgraduate education in psychiatry for the general physician at the universities and at the yearly assemblies of the state medical societies, the A.M.A., Southern Medical Association, and the American Academy of General Practice. The introduction of general physicians and their use in state institutions and other mental hospitals, a program already working in a number of states, is completely and educationally feasible.

We general physicians feel that we are just "too busy" to get involved with more intense psychiatry. This is not so. If the general physician's office is not run on the appointment basis, he might set aside one morning a week for a three hour period, or one evening, and give thirty minute appointments to the patients requiring more time for talking and unburdening themselves of their problems. These patients should be charged accordingly, and should be told why the fee must be a bit more than the usual office visit. Patients do not resent this forthrightness. If the general physician's office is on the appointment basis as many general physicians are, this simplifies the problem of time. One simply regulates the appointment time to suit the problem patients. A proper fee for the time spent is no barrier if the patient feels that by giving him the added and, I might add, undivided time you have helped him.

Gentlemen, whether we know it or not, psychiatry or psychosomatic medicine,—I like to call it "sitting and listening medicine" is with us for evermore. The liaison committees of the American Psychiatric Association and American Academy of General Practice were formed to evolve methods and procedures to increase the knowledge and ability of the general physician in the field of psychiatry. With such added knowledge we can hope to bring adequate psychiatry to all who need it.

The Health Department's Role in an Industrial Hygiene Program*

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This is an interesting demonstration of what can be done in organizing a health program for small industries through the medium of the local health department.

Introduction

DURING THE PAST DECADE, many programs have been developed in the use of multiple screening procedures. Some of these have been carried on by health departments for certain geographical areas, others with industrial groups. Most, if not all, of these programs were so organized that a large number of individuals were seen in a comparatively short time. This type of organization seemed unattainable by the health department working in a small population where a number of highly trained technicians would not be available. However, it seemed there might be some common meeting ground between multiple mass screening procedures by the local health department and many small industries in which some type of health service would not be utilized as a permanent part of their program.

This paper describes an attempt to meet in that common area.

Situation

The department which carried on this program serves a population of approximately 50,000. The largest city in the area has a population of approximately 21,000, another with 10,000, and two smaller areas of population of 4,000, and 2,500. In Kay County, Oklahoma, 40 industries were identified which could be served by the type of program planned. One or two were eliminated because of their comprehensive medical program. The others ranged in size from one with 3 employees to one with over 800 employees. Only 5 of the group had more than 100 employees.

This then, were the groups that would be reached with the program that was planned.

Community Organization

In planning the program, it was hoped to have it as self-contained as possible within the framework of the health department. One concession made to the program was the addition of one nurse to the regular staff of the health department. Since this would be a full-time job during the one year study period, it was not practical to add this to the duties of the already overworked nursing staff. The local tuberculosis association paid the salary of this nurse as their contribution to the community demonstration. Since electrocardiograms were not routinely done in the department, two of the local physicians volunteered to read the ECG's for this program. Otherwise, the program was carried on within the framework of the present health department staff and budget. Extra funds were not allocated to the department for this program.

The first stage in the planning was the approach to the medical society. Its approval was obtained for the program for one year on a demonstration basis. The final report on each individual examined was sent to the family physician named by the person examined, and the follow-up, in general, was left to the family physician.

In informing the employees and employers about the program, three approaches were used. Where the employees were organized into a recognized union, the union officials and, finally, the union membership were approached. This method was used in two of the industries. In both, the union members accepted the program, made appointments, and took the responsibility of seeing that the appointments were kept. In both instances,

*Read before the Section on Public Health, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

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too, the members of these unions came in for examination on their own time. Where personnel were not on shifts, they took sick leave to have the examination done. Another approach was made directly to the employer, who decided for or against participation in the program. If the employer decided that his employees should participate in the program he accepted the responsibility for appointments. The third approach was directly to the employees at the insistence of the employer. In approximately 50% of cases, employees were given time off at company expense for the program. In all instances, as far as the health department knew, this was a voluntary program for the individual. It was made clear at the beginning that the only individual report the health department made would be given to the family physician. The employers would not receive reports on individuals, nor would they receive a report on their employees as a group.

Procedures

Appointments were made for each individual at one hour intervals. During that hour, the following tests were done:

1. Height and weight were measured on diagnostic scales of the type usually found in physician's offices. As a basis for comparison, the table, "Desirable Weights for Men and Women of Ages 25 and Over," found in the Metropolitan Life Insurance Company pamphlet, *What Is Your Best Weight?* was used. The only variable factor in the use of this table is the decision by the examiner as to the size of frame (small, medium, or large) applicable to each subject.

2. Hemoglobin in per cent was calculated by the use of the Rouy photometer. In this procedure, 15.5 Gm. of Hgb. equal to 100% Hgb. for the normal male, and 14.2 Gm. of Hgb. is equivalent to 100% Hgb. for the normal female.

3. Blood pressures were taken after most of the other tests so that feelings of apprehension might not cause an increase in the normal pressure. Systolic pressures over 150 and below 100, and diastolic pressures over 90 and below 60 were considered abnormal in this program.

4. The urine sample examined was collected at the time of the appointment. Specific gravity was determined with the Fischer urinometer. Specific gravity below 1.010 was considered abnormal. *Clinitest* was used to determine the presence of sugar, while *Bumintest* was used to test urine for albumin. In both tests, results were read as negative, faint trace, trace, 1+, 2+, 3+, and 4+.

5. Blood samples were taken and sent in to the State Health Department Laboratories as a routine sample for serologic examination for syphilis.

6. Chest x-rays were done on 70 mm. film, and were developed and read by the State Department of Health. When large x-rays were requested, the 14×17 films were taken in our department, and developed and read by the State Department of Health. These were read for any chest disease usually seen in x-rays.

7. Vision was tested on the Bausch & Lomb Orthorator, and the standards provided with the machine were used. Where the standard showed a loss in vision, a copy of the report was given the subject. Vision was tested under the circumstances in which the subject worked. If glasses were used on the job, vision with glasses was tested.

8. Hearing was tested on the Puretone audiometer, and the per cent hearing loss was calculated on the audiogram produced by the Audio Development Company.

9. The ECG was made on the Direct Writing Burdick Electrocardiograph, and read by two physicians practicing in one of the local communities.

All reports on each individual were filed in a manila folder headed by that individual's name. When the results of all the tests were received by the department, a report was made and sent to the physician named by the subject. At the same time, the employee received one of two statements: (1) When all tests were considered within normal limits, he was so notified. This was done at the request of the medical society. (2) Where one or more of the tests was not considered within normal limits, the person was sent a notice which said that the results of the examination had been mailed to his family physician, and that he should see his family physician for interpretation of the results. In a few instances they were referred to their physician at the time of the examination. Specifically, when an abnormally high blood pressure was noted, the nurse would recommend that he see his physician immediately. In all cases where a hearing loss was noted, or where there was a loss of vision, a copy of the record was given to the employee and he was urged to take it to his physician.

The follow-up of the year's program was not begun until at the end of the test year. Each physician was asked two questions about each person who had been referred to him. On this questionnaire mailed to the physician, we also gave the date the individual was examined, as well as the abnormal findings. The two questions asked were:

"Has this individual seen you since the date he was examined?"

"What diagnoses were made as a result of the above tests?"

By these questions we were trying to determine,—first, how many people went to their physicians after the examination showed a defect present, and, second, if we had assisted in making new diagnoses by this program.

Results

1. *Number examined.* During the year this program was in progress, 913 individuals, representing 17 different industries, were given all or most of the tests mentioned. Of this group, 703 (77%) were found to have one or more abnormalities.

2. *Age.* The average age for this group was 38.8 years, and a distribution of from 18 years to 69 years was noted. The age distribution was as follows:

Below 19 years	26
20-29 years	199
30-39 years	252
40-49 years	249
50-59 years	143
60-69 years	38
Not stated	3
	910

Fifty-five per cent of this group were between 30 and 49 years of age.

3. *Sex.* Seventy-eight per cent of the persons were male.

4. *Height and weight.* Of these two factors, weight is the variable one. The amount of overweight or underweight was calculated on the basis of height and frame structure. On this basis, 24.8% were found to be overweight, and 5.3% underweight.

5. *Hemoglobin.* The hemoglobin per cent ranged from 70 to 120 per cent. The distribution of hemoglobin percentage was as follows:

Below 79%	2
80- 89%	40
90- 99%	466
100-109%	340
110-119%	50
120%	1
Not recorded	5
	904

6. *Blood pressure.* The following are the findings:

	Number	*Per Cent*
Normotensive	652	71.7
Hypertensive	225	24.7
Hypotensive	29	3.2
Not recorded	4	.4
	910	100.0

7. *Urinalysis.* In the test for *specific gravity,* there were 201 specimens that had an insufficient quantity of urine to use for the test. The findings were as follow:

Insufficient for test	201
Below 1.011	132
1.011-1.029	551
1.030 and over	21
	905

The results of the tests for urine *sugar* and *albumin* were as follow:

	Sugar	*Albumin*
No test	21	21
Negative	667	797
Faint trace	109	25
Trace	97	30
1+	7	23
2+	3	8
3+	1	1
	905	905

8. *Blood.* Only three positive blood tests were found in this group. Two were known and had had previous treatment. The other was a false positive. (The V.D.R.L. was the test used.)

9. *X-ray examination of chest.* Of the 816 x-rays made, 802 (98.3%) were negative. Nine were unsatisfactory, and the individuals did not return for a second one. One x-ray film showed a pulmonary lesion, one a calcified scar, and 3 an abnormal heart. The pulmonary lesion was that of an inactive case not formerly known to our department.

10. *Vision test.* The IBM card used with the orthorator contained much information which was obtained by the nurse before the actual test is given. This card was made to be used in industrial testing. In checking the results of the test, the company provided 6 standards covering the usual occupational groups seen in industry. For the purposes of this report, the loss in vision in each test was compared with a composite standard, made from these six. Information obtained by the nurse's questions was as follows:

Total number checked	909
Glasses not worn	430
Glasses always worn	231
Glasses irregularly worn	34
Glasses used on special jobs	19
Safety goggles worn	17
Bifocals worn	231
Prescription for far vision	318
Prescription for near vision	384

The actual tests gave the following results:

Test Given	*Far Vision*	*Near Vision*
Vertical	30	56
Lateral	83	108
Acuity, both eyes	65	254
Acuity, right eye	101	216
Acuity, left eye	89	208
Depth	106	
Color	51	

In comparing the orthorator test cards with the Snellen charts, it is noted that the 65 showing loss in far visual acuity for both eyes would have scored between 20/30 and 20/70 with a simple Snellen Test, while 182 more would show a beginning vision loss between 20/20 and 20/30. These last (182) were not included in the figures indicating a loss of vision. It would be interesting to recheck this group to see if this is the beginning of a greater visual loss or whether the loss has stabilized at this point.

11. *Hearing tests.* The results of the hearing tests have been grouped as follows:

Per Cent Loss	*Right Ear*	*Left Ear*	*Both Ears*
No hearing loss	208	198	218
Less than 10%	489	470	493
11%-25%	146	165	140
26%-50%	46	55	41
51%-99%	21	22	18
Total	910	910	910

It was noted by the nurse conducting the examinations that individuals in the same line of work presented essentially the same hearing patterns.

12. *Electrocardiogram.* The findings were as follow:

Normal ECG	508
Suggestive electrocardiographic evidence of myocardial infarction	3
Definite electrocardiographic evidence of myocardial infarction	2
ECG compatible with posterior infarct	1
Posterior infarction	1
ECG compatible with anterior infarction	1
Anterior infarction	1
No ECG given	86
Other findings	307
Total	910

During this period we had some trouble with external electrical interference which we could not locate. We were able to get most of the individuals affected to return at another time. Even then, we did not get electrocardiograms on 86 people. Normal electrocardiograms were found in 508. The figure under "other findings" includes 147 in which left axis deviation was noted, 67 with sinus bradycardia, 35 with sinus arrhythmia, 9 with bundle branch block, either right, left, or partial.

13. *Results of questionnaires.* As of this date, 703 questionnaires have been sent to the family physicians, and 617 have been returned. Of these 617, it was learned that:

140 did not see their physician after the examination.

477 did see their physician after being notified of the results.

260 were reported as having negative examinations.

217 had diagnosis made upon them.

31 had been diagnosed previously.

186 had new diagnoses made.

The results of the examinations were placed on IBM cards and are available for comprehensive analysis.

Cost of the Program

An important item in adding any new program to an already crowded schedule is the cost. The cost of this program includes the actual outlay of money necessary for the extra items in the program. Items such as utilities, office space, time of the health officer, nursing supervisor, or clerks were not considered in estimating this cost. The estimated total cost to the local health department and the county tuberculosis association was about $3,800. This makes each examination cost $4.16, which is well above the average cost for most screening programs, and was expected. As more time is necessary for each examination the cost increases. This was anticipated in this particular program.

Suggested Program

It is not believed that this program should necessarily be used in local health departments to the extent described here. The amount of time and personnel devoted to the program depends upon the number and size of industries in the community which participate in the program, as well as the size of the health department.

A most important and necessary consideration is the acceptance and participation in it by the local medical society. This program was based on the active participation of the individual family physician in the follow-up on his patients. It certainly would not be satisfactory to do these tests and then leave the

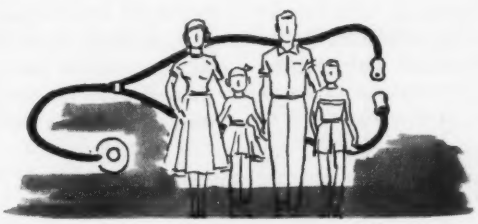
patient without any recommended action. It must be remembered that some of these tests are simple screening procedures, and that no attempt was made to arrive at a definitive diagnosis by the local health department.

This program could be adopted by the small health department using the nurses who are providing a general public health nursing service to the community. It should be financed by the industries which should require their personnel to take the examination. It is visualized: (1) as a part of a preemployment physical examination where the family physician (or a physician hired by the industry on a part-time basis) is used, or (2) as a continuous screening program of those already employed. The consideration for a new program has been based on the first of these two possibilities.

In most cases, it would be necessary to increase the staff of the health department by at least one nurse. This nurse would be included as a staff member, given a nursing district and started on a general public health nursing service. The times for the examinations would be set up as are all other conferences or clinics in the health department, the amount of time given to them depending upon the participation by the local industries. Appointments would be made for certain half-day periods, and one of the nurses assigned to that particular period, just as she may be assigned to other work in the department. In this way, the nurse would become familiar with the tests and could discuss them better if a home visit were necessary. If the participation were such that over 50% of the time were needed for this testing, consideration should be given to providing personnel on a full-time basis.

Summary

A demonstration program in industrial hygiene was planned and executed in an attempt to discover a possible program suitable to the health department working with small industries. On the basis of incomplete follow-up, new diagnoses were made on 13% of those examined. A suggested program is discussed.



The Clinical Pharmacology of Hydrochlorothiazide

RALPH V. FORD, M.D.,* *Houston, Tex.*

The results with a new diuretic of the benzothiadiazine group are described herein. It seems as if this drug may have less tendency to influence certain electrolytes in an untoward fashion than other members of this chemical group, but the ultimate answer on this will depend upon a greater use in a variety of diseases requiring diuretic therapy.

HYDROCHLOROTHIAZIDE† is the newest member of that unique family of benzothiadiazines which have been found to be of value in the management of cardiovascular-renal disease. The first member of this family was chlorothiazide which has been widely studied and clinically evaluated with gratifying results in the management of various edematous states and as an adjunct in the therapy of hypertension. Chemically, hydrochlorothiazide (Fig. 1) differs from chlorothiazide in having no double bond in the heterocyclic ring. It has been shown to be at least ten times as potent as chlorothiazide (in terms of natriuretic effect) when given intravenously to dogs.[1]

The purpose of the present communication is to report the clinical pharmacology of hydrochlorothiazide in terms of its potency as a diuretic agent, its effects on the urinary excretion of various electrolytes, its behavior in terms of onset and duration of action, its influences on serum biochemical architecture, and finally, its value in edematous states of varied etiology as well as in the treatment of hypertension.

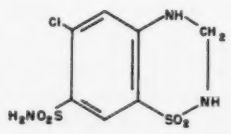
Materials and Methods

A. Dose Response Curve. A pilot study of hydrochlorothiazide was undertaken to determine the dose response curve using previously described technics for the bio-assay of diuretics.[2] Briefly described, the subjects of this study were 10 men with hypertensive cardiovascular disease who were maintained under controlled metabolic conditions. They ate a diet which contained 50 mEq. of sodium and drank 3,000 ml. of distilled water per day. All medications other than diuretics necessary for the control of their congestive heart failure were maintained. At the time of the study they were free of detectable edema. Twenty-four hour urine specimens were collected and analyzed for sodium and volume. Their weights were obtained prior to breakfast and after voiding. The particular dose of the drug was given at 6 a.m. each morning. The dose of hydrochlorothiazide was given in progressively incremental amounts beginning with 12.5 and extending to 200 mg. as a single dose. This was given five times at each dose.

B. Determination of Potency. After the significant points of the dose response curve were established by a pilot study, namely between 25 and 50 mg., the drug was administered at both of these doses to each of the 10 subjects of the study and the previously described observations were made. These data were then subjected to the statistical analysis

FIG. 1

STRUCTURAL FORMULA OF HYDROCHLOROTHIAZIDE



6-CHLORO-7-SULFAMYL-3, 4-DIHYDRO-1, 2, 4-BENZOTHIADIAZINE-1, 1-DIOXIDE

The structural formula of hydrochlorothiazide reveals that it differs from chlorothiazide in having no double bond in the heterocyclic ring.

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With the technical assistance of Joan Bush.

†Hydrochlorothiazide is 6-chloro-7-sulfamyl-3, 4-dihydro-1, 2, 4-benzothiadiazine-1, 1-dioxide. Available from Merck & Co., Inc. as Hydrodiuril.

of variance for the determination of significance. A computation of the "potency estimation" was then made. These data were subsequently compared to the standard diuretic, meralluride (Mercuhydrin), which has a potency of "one."

C. Electrolyte Excretion Effects. The urinary electrolyte excretion effects were studied following the administration of hydrochlorothiazide in five different patients, each of which received doses of 25, 50, and 100 mg. at intervals of 5 days. These studies consisted of the analysis of the urine for volume, sodium, potassium, ammonia, pH, chloride, bicarbonate, titratable acidity, and total solute in six fractional periods during the 24 hours following the administration of each dose (three consecutive two-hour periods followed by three consecutive six-hour periods).

D. The Effect of Hydrochlorothiazide after Daily Administration on Body Weight, Sodium Excretion, and Serum Biochemical Architecture. The drug was administered at a dose of 25 mg. daily to 10 patients for 7 consecutive days. The urine was analyzed for sodium and volume, and the blood was analyzed for significant electrolyte changes (sodium, potassium, chloride, bicarbonate, urea nitrogen, and hematocrit). Body weight was determined daily. The purpose of this study was to determine whether the drug is repetitively effective and that tolerance to the drug does not develop, as well as to evaluate its effects on the biochemical architecture.

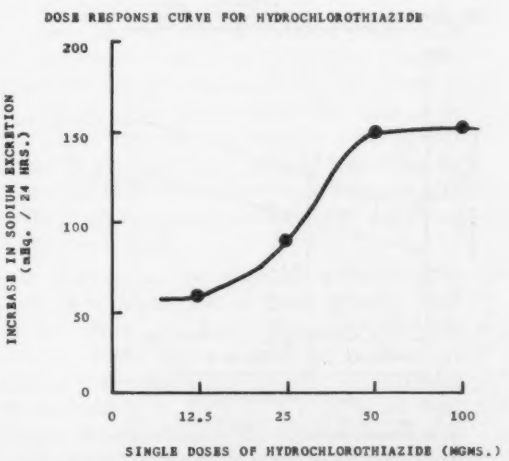
E. Preliminary Observations on Hydrochlorothiazide in Various Edematous States. Hydrochlorothiazide was given to patients with edema (mild to moderate) of varied etiology in a dose of 25 mg. daily for 21 days and observations were made in the control state, and at the end of 7 and 21 days, of body weight, serum electrolytes (sodium, potassium, chloride, and carbon dioxide combining power) as well as blood urea nitrogen and hematocrit. There were 10 patients with cardiac edema, one with nephrotic edema, 5 with edema induced by steroid therapy, one cirrhotic with mild edema and moderate ascites, and 5 women in the third trimester of pregnancy.

F. Preliminary Observations on the Effectiveness of Hydrochlorothiazide in Antihypertensive Therapy. Five patients in each of 4 groups were given hydrochlorothiazide in a dose of 25 mg. daily for 3 weeks. The first group consisted of patients with hypertension who had been observed for 3 consecutive weeks prior to therapy. The second group consisted of patients who were receiving Rauwolfia (Raudixin 100 mg. daily b.i.d.) for a period in excess of 3 months. The third group consisted of patients who had been receiving Rauwolfia in addition to mecamylamine (in ganglionic blocking doses) but who were less than optimumly controlled for a period in excess of 3 months. The fourth group consisted of patients who had been fairly well controlled on a regimen consisting of Rauwolfia, mecamylamine, and chlorothiazide (500 mg. daily). In this group, hydrochlorothiazide was substituted for the previous chlorothiazide therapy in a dose of 25 mg. Observations were then made at the end of the first and third week.

Results

A. Dose Response Curve. The pilot study revealed that there was a slight increase in sodium excretion beginning with even the smallest dose (12.5 mg.) but that the significant part of the response curve was between the 25 and 50 mg. dose. Although the 100 and 200 mg. doses were not associated with evidences of clinical toxicity, the sodium excretion did not increase significantly beyond that observed with the 50 mg. dose (Fig. 2).

FIG. 2



The dose response curve of hydrochlorothiazide illustrates that the effective dose range is between 25 and 50 mg.

TABLE 1

DIURETIC RESPONSES TO SINGLE DOSES OF HYDROCHLOROTHIAZIDE
(Averages of determinations on 10 patients)

	25 Mg.				50 Mg.			
	C	D	I	P value*	C	D	I	P value
Urine Volume (L/24 hrs.)	3.0	3.4	0.4	<.01	3.0	4.2	1.2	<.01
Urine Sodium (mEq/24 hrs.)	45	135	90	<.001	47	197	150	<.001
Body Weight (Kgs.)	55	54.6	−0.4	<.01	54	52.9	1.1	<.01

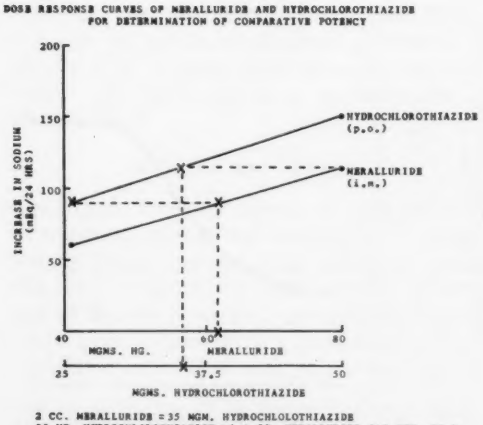
Key:
*P value—Determined from Student's "t" test.
C—Control
D—Drug
I—Increase

B. Determination of Potency. Ten observations at two doses (25 and 50 mg.) revealed there was a significant increase in the urinary volume and the urinary sodium and a decrease in weight (Table 1). The average increase in urinary sodium was 90 mEq/24 hours over control at the 25 mg. dose. At the 50 mg. dose the average increase was 150 mEq/24 hours over control. These changes, of course, are paralleled by changes in urinary volume and weight loss.

After the data had been subjected to an analysis of variance, it was found that the dose response curve for hydrochlorothiazide and meralluride are parallel and linear and that the error is not significant (Fig. 3). By direct reading of the curve it is seen that a dose of 25 mg. of hydrochlorothiazide orally administered is equivalent in natriuretic potency to 1.6 cc. of meralluride (Mercuhydrin) administered intramuscularly. Expressed in another way, 2 cc. of meralluride is equivalent to 35 mg. of hydrochlorothiazide. The data revealed that the potency estimation of hydrochlorothiazide is 1.4 while meralluride is 1.0. In other words, hydrochlorothiazide is 1.4 times as potent as meralluride at the two doses under observation.

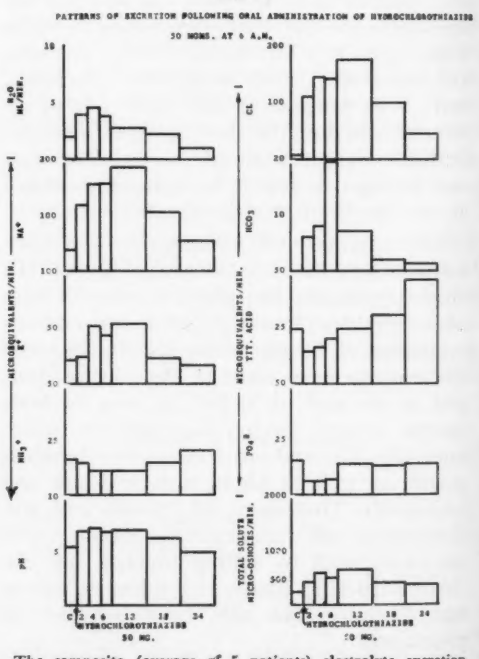
C. Electrolyte Excretion Effects (Fig. 4). A

FIG. 3



The potency estimation of hydrochlorothiazide is 1.4 (that is, it is 1.4 times as potent as meralluride at the doses observed).

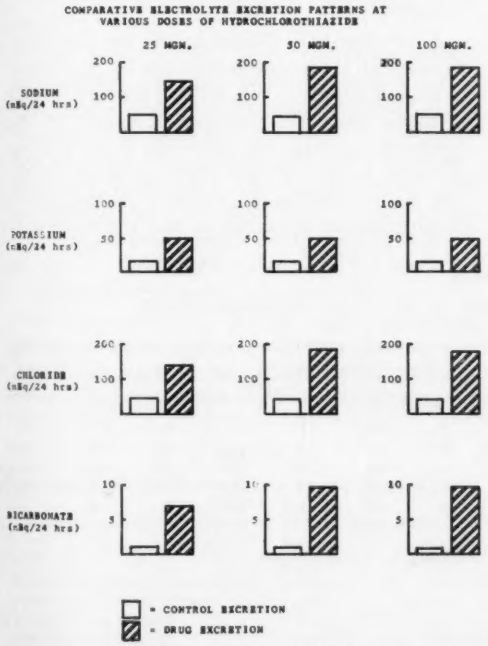
FIG. 4



The composite (average of 5 patients) electrolyte excretion effects demonstrate that the predominant effect is on sodium and chloride. The kaliuretic effect is less than one-fourth as great as the natriuretic effect. There is an increase in bicarbonate excretion. However, the 24 hour loss of the latter two ions is not significant.

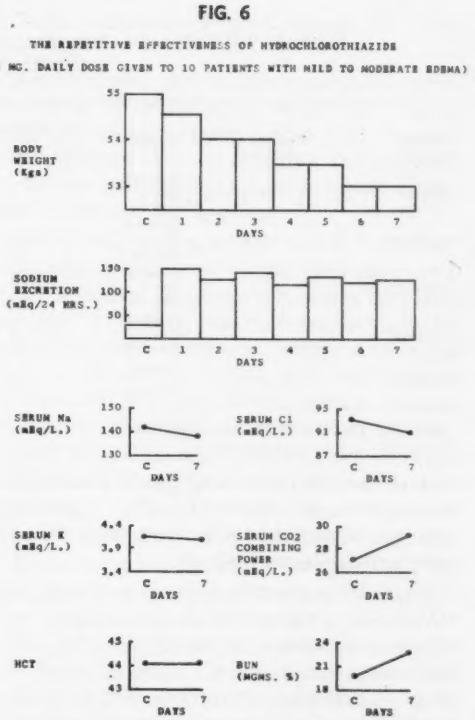
composite electrolyte excretion pattern (average of 5 patients) at the 50 mg. dose level of hydrochlorothiazide revealed that there is an increase in all moieties except ammonia occurring during the first two hour administration of the drug, but the increase reached a maximum between the sixth and twelfth hours following the drug. These changes persisted for at least 18 hours and returned to control levels within the 24 hour period. Ammonia excretion was characterized by a compensatory decrease during the period of response to the drug and a slight increase at the end of the 24 hour period. The most significant increase in excretion rates were observed in sodium and chloride which showed a six to eightfold change while the increase in potassium excretion was about one-fourth or less that of sodium and chloride. Although there was a slight increase in the rate of bicarbonate excretion, its average total excretion over the 24 hour period was small. No significant alteration in the excretion of phosphate or titratable acidity was observed. The pH of the urine increased slightly during the period of drug activity.

FIG. 5



Comparison of the significant electrolyte excretion effects of hydrochlorothiazide at increasing dosages indicates that the sodium and chloride response is proportional to the dose. However, the effect on potassium and bicarbonate excretion is no greater at the larger doses resulting in a declining sodium : potassium ratio at the higher doses.

FIG. 6


THE REPETITIVE EFFECTIVENESS OF HYDROCHLOROTHIAZIDE
(25 MG. DAILY DOSE GIVEN TO 10 PATIENTS WITH MILD TO MODERATE EDEMA)
BODY WEIGHT (Kgs)
SODIUM EXCRETION (mEq/24 HRS.)
SERUM Na (mEq/L.)
SERUM Cl (mEq/L.)
SERUM K (mEq/L.)
SERUM CO2 COMBINING POWER (mEq/L.)
HCT
BUN (MGMS. %)
DAYS

The persistence of weight loss and sodium excretion following 7 consecutive days of therapy with hydrochlorothiazide indicates that tolerance to the drug does not develop. Although there is a tendency toward the development of hypochloremic alkalosis, this is not clinically significant. The changes in blood urea nitrogen and hematocrit are also not siginificant.

There were certain differences observed in the electrolyte excretion patterns at various doses of hydrochlorothiazide ranging from 25 to 100 mg. (Fig. 5). Although the rates of excretion for sodium and chloride were proportional to the dose, the rates of excretion for potassium and bicarbonate were relatively less at the high dosages (especially 100 mg.) than at the lower dose.

D. The Effect of Hydrochlorothiazide after Daily Administration on Body Weight, Sodium Excretion, and Serum Biochemical Architecture. There was a continuing excretion of sodium following daily therapy with hydrochlorothiazide as well as a decline in body weight. No significant changes in blood urea nitrogen and hematocrit were observed. There was a tendency toward slight elevation of the

TABLE 2

CLINICAL RESPONSES TO HYDROCHLOROTHIAZIDE IN VARIOUS EDEMATOUS STATES
(Average values for each group)
(Dose of 25 mg. daily)

Type of Edema	Number of Patients	Period	Cumulative Weight Loss (lbs.)	Serum (mEq/L) Na	K	CO^2 C.P.*	Cl	BUN Mg. %	Hct
Cardiac	10	Control		140	4.2	28	105	18	45
		Day 7	3	137	4.1	30	103	20	46
		Day 21	10	137	4.1	31	102	21	47
Nephrotic	1	Control		130	3.7	23	92	30	39
		Day 7	6	125	3.4	24	91	31	41
		Day 21	14	124	3.4	25	89	28	43
"Steroid"	5	Control		148	3.3	31	91	15	39
		Day 7	2	146	3.1	31	90	17	41
		Day 21	5	145	2.9	36	86	18	42
Cirrhotic	1	Control		130	3.0	25	89	10	40
		Day 7	5	128	2.5	24	85	11	41
		Day 21	14	127	2.5	26	85	11	40
Pregnancy	5	Control		142	4.3	28	103	12	38
		Day 7	2	141	4.2	30	101	13	39
		Day 21	4	140	4.1	32	101	14	40

*CO^2 C.P.—Carbon dioxide combining power.

carbon dioxide combining power but this was moderate and not clinically significant. Changes in sodium, potassium, and chloride were not significant (Fig. 6).

E. Preliminary Observations on Hydrochlorothiazide in Various Edematous States. The effectiveness of hydrochlorothiazide as a diuretic agent in edematous states of varied etiology is demonstrated in table 2. The greatest weight loss was observed in the patients with nephrotic edema and cirrhotic edema. Significant changes, however, occurred in the other three groups as well, i.e., cardiacs, pregnancy, and edema induced by steroid therapy. Changes in the biochemical architecture of serum were observed in the direction of the hypochloremic alkalosis in all five groups and was most pronounced in the patients with edema induced by steroid therapy. There was a definite decline in the serum potassium in the cirrhotic patient but this patient had the lowest control level of serum potassium. None of these changes were reflected in a change in clinical status of the patient except for the gratifying relief of edema in all patients observed.

F. Preliminary Observations on the Effectiveness of Hydrochlorothiazide in Antihypertensive Therapy. When hydrochlorothiazide is made the sole therapeutic agent in the treatment of mild hypertension there is a significant decline of the blood pressure at the end of the third week (Table 3). When hydrochlorothiazide is added to the previous anti-

TABLE 3

THE EFFECT OF HYDROCHLOROTHIAZIDE AS AN ANTIHYPERTENSIVE AGENT
(Average values for 5 patients in each group)

Antihypertensive Regimen in the "Control" State	Blood Pressure* Control S	D	MBP	Drug** First Week S	D	MBP	"P"	Third Week S	D	MBP	"P"
None	190	110	137	160	90	113	.05	150	90	110	<.001
R[1]	160	105	120	150	80	103	.05	140	80	100	<.001
R + GB[2]	140	100	113	130	85	100	.05	130	70	90	<.001
R + GB + C[3]	140	90	107	140	85	103	N.S.	140	85	103	N.S.

KEY:
*Blood pressure values are recorded in the upright position.
**Drug—Values after addition of hydrochlorothiazide 25 mg. daily.
S—Systolic.
D—Diastolic.
MBP—Mean blood pressure (diastolic plus one-third the pulse pressure).
"P"—P values derived from Student's "t" test.
[1]R—Rauwolfia alone (Raudixin 100 mg. twice daily).
[2]R + GB—Rauwolfia plus mecamylamine in ganglionic blocking doses.
[3]R + GB + C—Rauwolfia plus mecamylamine and chlorothiazide (500 mg. daily) (hydrochlorothiazide replacement for chlorothiazide in a dose of 25 mg. daily).

hypertensive regimen of Rauwolfia alone, or Rauwolfia in combination with mecamylamine, there is an additional reduction in blood pressure but to a lesser degree than in the former group. When hydrochlorothiazide is used as the replacement for chlorothiazide in the adjunctive management of severe hypertension which is treated with Rauwolfia plus ganglionic blocking agents (mecamylamine), there is no significant difference between these two compounds.

Discussion

The data of the current study indicate that hydrochlorothiazide is a potent saluretic agent that resembles chlorothiazide qualitatively but is several times more active. In humans, under the conditions of this study, it appears that 25 mg. of hydrochlorothiazide is equivalent to approximately 2,000 mg. of chlorothiazide. Its position in the scale of relative potency among diuretic agents is revealed in table 4. It is interesting to note that hydrochlorothiazide, an orally effective agent, is more potent than the usual maximal dosages of parenterally administered organo-mercurial diuretics.

The urinary electrolyte excretion effects demonstrate that the primary action of this drug is to decrease the renal tubular reabsorption of sodium and chloride. The urinary loss of potassium and bicarbonate following this drug is relatively less than that seen with chlorothiazide. This has clinical implications in that the problem of hypokaliemia will be much less. Although there is a tendency toward the development of hypochloremic alkalosis this same effect is seen in other equally potent diuretic agents including the organomercurials as well as chlorothiazide. Under the conditions of this study no clinically significant syndrome of hypokaliemia has been observed.

TABLE 4

COMPARISON OF POTENCY OF VARIOUS DIURETIC AGENTS

Drug	*Route of Administration*	*Potency Estimation**
Hydrochlorothiazide (Hydrodiuril)	Oral	1.4
Meralluride (Mercuhydrin)	I.M.	1.0
Chlorothiazide (Diuril)	Oral	0.8
Flumethazide (Urolog)	Oral	0.7
Mercaptomerin (Thiomerin)	I.M.	0.5
Chlormerodrin (Neohydrin)	Oral	0.5
Acetazoleamide (Diamox)	Oral	0.25

*Determined from previous analysis of variance of these drugs.[2]

The absence of the development of tolerance (Fig. 6) to this drug following consecutive daily administration is of definite benefit. This indicates that the drug can be used daily in the treatment of moderate to severe edema with repetitive effectiveness.

The widespread potential use of hydrochlorothiazide is indicated by the data showing it to be effective in edematous states of varied etiology. The drug was effective in inducing a diuresis and subsequent weight loss in patients with cardiac edema, nephrotic edema, cirrhotic edema and ascites, edema induced by steroid therapy, and the edema of pregnancy. Although the tendency toward hypokaliemia is most marked in the patient with cirrhosis, this is of a lesser order of magnitude than that observed with chlorothiazide.

Since attention has been directed to all diuretic agents as having potential antihypertensive properties, it is only natural that hydrochlorothiazide should be expected to present similar attributes. Thus, hydrochlorothiazide is effective not only in the management of the hypertensive state as the sole therapeutic agent but is also of value in augmenting the antihypertensive effects of Rauwolfia and ganglionic blocking agents (Table 3).

Conclusions

Hydrochlorothiazide is a potent diuretic agent with pharmacologic effects of such a nature as to indicate that it is more safe than currently available agents. It is at least 20 times more potent (on a weight of drug basis) than chlorothiazide and is 1.4 times as potent following oral administration as meralluride following parenteral administration. The tendency to produce disturbances in the biochemical architecture is much less because of its predominant effect upon the excretion of sodium and chloride and a much lesser effect on the excretion of potassium and bicarbonate. It is effective in edematous states of varied etiology as well as in the management of the hypertensive state.

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Fluothane: A New Nonexplosive Volatile Anesthetic Agent — Preliminary Report on 2,000 Administrations*

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An extensive experience with this new anesthetic drug demonstrates its advantages if given under careful supervision or by experienced anesthetists.

ONE OF THE MOST PROMISING DRUGS recently synthesized[1] in the constant search for a more perfect anesthetic agent is Fluothane—a halogenated ethane, 2 bromo—2 chloro—1:1:1 trifluoroethane having the structural formula:

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    F     BR
F   C-C   CL
    F     H
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It is a clear volatile liquid which mixes well with oxygen and is not explosive or flammable (Table 1). The odor is pleasantly sweet and the vapor can be inhaled without irritation. Applied to the skin Fluothane produces no irritation as does ether or chloroform. It is a stable compound even in the presence of soda lime but in time breaks down into various halide acids if exposed to light, moisture, or air.

The drug has been studied sufficiently in animals[2-4] with good results, to warrant further study on humans. After reviewing the work reported,[1-16] representing over 5,000 administrations, and observing its use at one of the University medical centers, we decided to give the agent a trial on the type of anesthesia required at our 300 bed hospital. This is a preliminary report of our clinical observations on the use of Fluothane as the principal anesthetic in 2,000 administrations.*

Technics

Fluothane may be administered by any technic that can be used with ether anesthesia. Table 2 shows the methods we used. The drug is twice as potent as chloroform and four times more potent than ether[3] therefore, in order to safely and accurately administer such a powerful anesthetic agent we found that a vaporizer which delivered the most accurate percentage was essential (Table 3).

One thousand three hundred and eighty-six of this series of anesthetics were given by the semiclosed technic receiving Fluothane by the copper kettle of Foregger which maintains the temperature of the vaporizing liquid constant and accurately delivers from 0.6 to 8.4 per cent. We also used the Heidbrink ether vaporizer with the regular ether bottle containing a wick placed on the inhalation side of the circle, but found the percentage delivered was not constant due to changes in the fluid level, the temperature and the variation of amount of gas being directed through the Fluothane at the same setting with different machines. With the fluid level above the bottom of the wick alarmingly high concentrations are obtained which are relatively uncontrollable, while with the wick removed almost no agent comes through the circuit, thus making it difficult to obtain a known percentage and even level of anesthesia. An attachment for standard gas machines is being perfected which will accurately measure Fluothane percentages from 0.10 to 5.0% and will soon be on the market.*

Most workers reported a 4 liter flow,—2 nitrous and 2 oxygen. We chose to use a 3:1.2 nitrous oxide mixture thus utilizing more of the analgesic effect of nitrous oxide and allowing a lower concentration of Fluothane but still providing adequate (about 30%) oxygenation. We were able to maintain ade-

*Read before the Section on Anesthesiology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

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Fluothane is produced by Imperial Chemical Industries Limited, Pharmaceutical Division, Manchester, England. A generous supply was provided for trial for this study by Ayerst Laboratories, New York, N. Y.

*The size of this series has been enlarged since the original presentation of the paper.

*F.N.S. vaporizer, Newton Instrument Co., Durham, N. C., now produces this vaporizer.

TABLE 1

PHYSICAL PROPERTIES

Anesthetic	Type	Chemical Formula	Molecular Weight	Boiling Point	Specific Gravity-Liquid (Water=1)	Solubility in 100 Parts Water	Solubility Oil-Water 37°C.	Limits of Flammability Air	Limits of Flammability Oxygen	Vapor Tension at 20°C. mm. Hg.
Ether	Diethyl-ether	$(C_2H_5)_2O$	74.12	34.6	0.715	7.5	3.2	1.85–36.5	2.10–82.0	439
Vinethene	Divinyl-ether	$(C_2H_3)_2O$	70.9	28.3	0.774	4.0	41.3	1.7 27.0	1.85 85	
Vinamar	Ethyl-vinyl-ether	C_2H_5-O-C_2H_3	72.10	35.8	0.759		45		2.1	4.85
Fluroramar	Fluorinated hydrocarbon	CF_3-CH-O-CH_2	126.0	42.7	1.13	0.4	94	3.0		
Fluothane	Halogenated ethane	CF_3-CH-Br-CL	197.39	50.2	1.86	0.345	330	Non-inflammable with O_2 0.5-50.0		233
Chloroform	Chlorinated hydrocarbon	CH CL_3	119.39	61.26	1.49	0.822	100			

quate anesthesia on a concentration ranging between 0.6 and 1.0% Fluothane vapor with this technic. Others reported maintenance concentrations of 0.8 to 2.5% necessary.[2,3,9,10] We did not use the closed circle absorption technic in this study though it has been reported.[3,4,7]

About 5 to 10 minutes prior to completion of the operation Fluothane was turned off completely and only nitrous oxide-oxygen 3:1.2 given in order to eliminate as much of the Fluothane as possible. Table 4 shows over half of the patients in this series recovered consciousness in the operating room. Another 657 were conscious enough to open their eyes on request in 3 to 5 minutes. In most instances the patients would fall asleep again and rest quietly 20 to 40 minutes depending on the length of the anesthesia, unless stimulated. There was noticeably less nausea and vomiting following Fluothane. Excitement was rare. In using the open drop technic (Table 2) in this study we found it particularly useful in children but experienced considerable difficulty in maintaining an even plane of anesthesia by this method. By blowing a 3:1.2 mixture of nitrous oxide oxygen with Fluothane 1.0 to 1.5% under the mask this open technic was smoother and it was easier to maintain an even plane of anesthesia. A striking feature of Fluothane was its lack of irritation; even when given by the open drop technic to the unpremedicated patient there was infrequent coughing, salivation or increased tracheobronchial secretions. The patient was warm and dry and pink showing peripheral dilatation. The induction was fast (usually less than 2 minutes) and if an excitement stage developed it was transient.

TABLE 2

TECHNICS OF ADMINISTRATION OF FLUOTHANE

Semiclosed circle absorber (Copper Kettle)	1,386
Semiclosed circle absorber (Heidbrink)	385
Open drop	65
Open drop + under mask insufflation	77
Nonrebreathing	76
Combination	11
	2,000

Cardiovascular System

With Fluothane, vagal action on the heart predominates, perhaps explaining the slowing of the pulse, the lowering of the systolic blood pressure more than the diastolic resulting in

TABLE 3

COPPER KETTLE VAPORIZER
FLUOTHANE CONCENTRATIONS

(200 cc. Liquid Fluothane in Vaporizer)

O_2 per kettle (cc./min.)	Approximate cc. Vapor Delivered	Approximate (± 0.05%) % Vapor at Gas Flows Bypassing Kettle 4 Liters/min.*	8 Liters/min.
50	23	0.6%	0.3
80	40	0.8	0.5
100	46	1.2	0.6
150	69	1.6	0.8
200	107	2.5	1.3
250	132	3.0	1.6
300	155	3.5	1.8
350	184	4.0	2.2
400	205	4.4	2.4
450	235	5.0	2.7
500	260	5.5	3.0
600	288	6.0	3.2
700	322	6.5	3.6
800	380	7.3	4.2
900	414	7.8	4.5
1,000	460	8.4	4.9

*Generally used as equal parts of oxygen and nitrous oxide but may be used as oxygen alone.

Data based on initial concentrations at temperature 24°C. and at 760 mm. Hg. pressure. Temperature drop insignificant at Vaporizer oxygen flows of 250 cc./min. or less.

TABLE 4

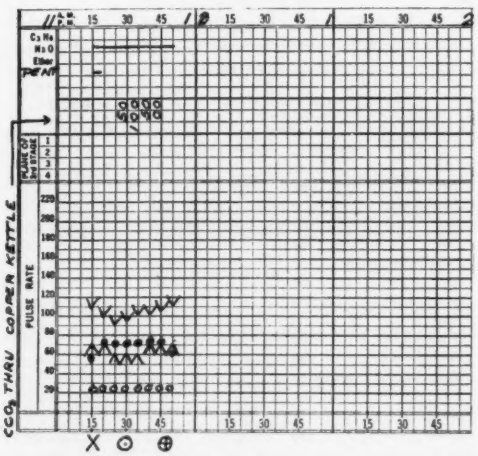
RECOVERY TIME FOLLOWING FLUOTHANE

In the operating room	1,096
3-5 min.	657
5-10 min.	129
10-20 min.	60
20-30 min.	52
30 min. or more	6
	2,000

reduced pulse pressure. The fall in blood pressure appears to be in direct proportion to the concentration of the vapor and especially the rate at which the concentration is increased. In patients in whom anesthesia is induced with one of the intravenous barbiturates and the introduction of Fluothane is withheld until the patient recovers from the initial fall of blood pressure caused by the barbiturate, there is very little subsequent fall in blood pressure, provided the Fluothane is introduced slowly (0.60 to 1.0%) (Figs. 1 and 2). In patients induced with nitrous oxide-oxygen mixtures and when the vapor is increased gradually there is little or no fall in blood pressure. The blood pressure is one of the most important guides to the level of Fluothane anesthesia.

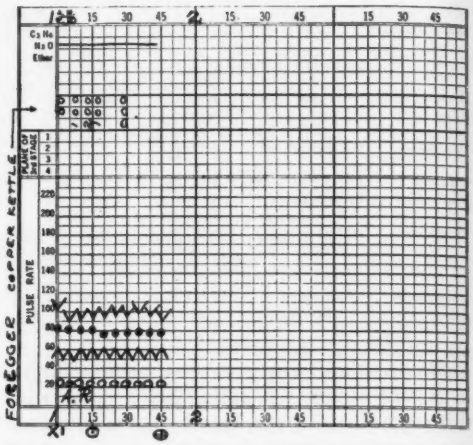
Arrhythmias such as nodal, bradycardia, bigeminal and extrasystoles do occur with Fluothane anesthesia, especially with rapid induction or deep levels, but can be prevented if the concentration of the vapor is decreased or if the induction is slow. Not more than 8% of the patients in this series were found to develop any arrhythmia clinically. We found its occurrence less as we gained more experience and skill in administration of the drug.

FIG. 1



Excision of breast tumor in a 36 year old woman. The initial fall in B.P. from Pentothal induction is shown. No depression occurred when the Fluothane was slowly introduced. (Premedication consisted of Nembutal gr. 1½, morphine gr. ¼, scopolamine gr. 1/200.) The patient awakened in 5 minutes.

FIG. 2



Iridectomy for acute glaucoma in a 32 year old woman. No barbiturate was used for induction. Only a slight fall in B.P. occurred when Fluothane was slowly introduced. (Premedication consisted of morphine gr. ¼ and scopolamine gr. 1/200.) The patient awakened in the operating room.

The diminished bleeding of all but the large arterioles under Fluothane anesthesia is one of its important properties. It does not seem to depend on hypotension because bleeding was minimal when the blood pressure was still near the preoperative level.

Postoperatively, in the recovery room, there was no vascular collapse as is seen sometimes following cyclopropane anesthesia. The patients were warm, dry and pink, and only 10% had blood pressures 20 to 30 mm. lower than the preoperative level which were readily corrected by elevation of the foot of the bed or by vasopressors such as methedrine. The postoperative circulation was better than that observed after the use of other anesthetics as there were no tremors or blueness of the extremities. The peripheral circulation and blood pressure were stabilized near the normal preoperative level.

Because of the ease with which fluctuation in blood pressure can be produced simply by increasing or decreasing the concentration of

the Fluothane vapor, it is possible that this drug may be superior to the hexamethoniums for inducing a controllable hypotensive state.

Respiratory System

Fluothane inhalation produces some degree of respiratory depression. When tidal and minute volumes were measured Chang[3] found they increased as unconsciousness occurred. As the level of anesthesia is deepened the respiratory rate becomes faster (30 to 40 per min.) and more shallow, sharply decreasing the tidal and minute volume. Further deepening leads to complete apnea. On lightening the anesthesia again the patient readily resumes spontaneous breathing.

We believe that in using any anesthetic agent which depresses respiration, whether it be cyclopropane or Fluothane, effective manually assisted respiration should be done. One of its desirable properties is the ease with which respiration can be controlled and spontaneous respiration be resumed when desired. One must be sure to reduce the concentration of the vapor when assisting respiration or else too deep an anesthesia will quickly result.

Although there were but 8 known asthmatics in this series none exhibited stridor, spasm of the larynx or bronchi. The decrease in salivary and bronchial secretions under Fluothane anesthesia, even without premedication, should decrease postoperative pulmonary complications since these most often have their beginning from retention of respiratory secretions caused by the anesthetics, a muscarine effect of the relaxants, parasympathomimetic drugs or painful reflexes. Fluothane depresses the cough and bronchoconstrictor reflexes, even those induced by the laryngoscope or endotracheal tube.

TABLE 5

DISTRIBUTION ACCORDING TO AGE

Age	*Number of Patients*
0-1 yr.	18
1 to 10 yrs.	290
11-20 yrs.	196
21-30 yrs.	450
31-40 yrs.	405
41-50 yrs.	316
51-60 yrs.	178
61-70 yrs.	117
71-80 yrs.	32
80 + yrs.	0
	2,000

TABLE 6

TYPES OF OPERATIONS DONE UNDER FLUOTHANE

Abdominal	486
Genitourinary	202
Orthopedic	174
Hernia	100
Neurosurgical	
Crainotomy	17
Disc	57
Other	19
Breast	72
Chest	9
Obstetrical	140
Vaginal	340
Rectal	79
Neck	41
Tonsillectomy	19
Eye	92
Extremity	83
Dental	70
	2,000

Clinical Use

Fluothane was used as the principal anesthetic agent in all ages and in almost every type of surgical procedure (Tables 5 and 6). It is agreed among those having used Fluothane that the fall in blood pressure is proportional to the concentration of the vapor; therefore we did not attempt to obtain deep relaxation, when required, by increasing the percentage but rather attained it by using the muscle relaxant, succinylcholine (Table 7). Other muscle relaxants were not used because of the profound fall in blood pressure reported when such relaxants were used with Fluothane in amounts sufficient to produce relaxation.

We noted that after Pentothal (average 200-250 mg.) induction before Fluothane and nitrous oxide-oxygen there was a more frequent mild (5 to 15 mm. Hg.) fall in blood pressure than when Fluothane in nitrous oxide-oxygen mixtures was given without Pentothal (Figs. 1 and 2). In either case, however, on continuing the anesthesia with the same Fluothane concentration the blood pressure returned in a few minutes to its normal level. It probably should not be introduced into the mixture until the fall of blood pressure from the barbiturate induction begins to return. We noticed that the awakening time was prolonged in patients who had received one of the barbiturates in addition to the regular premedication. Premedication was the usual proportion of morphine or Demerol with scopolamine or atropine, with or with-

TABLE 7

FALL OF BLOOD PRESSURE DURING FLUOTHANE INDUCTION

B. P. Fall (mm. Hg.)	*Number of Patients*
None	972
5-10	523
10-20	249
20-30	49
30-40	5
40 +	3
	1,801

out one of the barbiturates. Premedication only for its drying effect is not necessary because there is little or no salivation in the unpremedicated patient receiving Fluothane. Since the drug sometimes tends to produce bradycardia, atropine or scopolamine should be given beforehand to prevent this. If bradycardia or other arrhythmias appear they can be abolished readily by intravenous atropine which also usually raises the blood pressure.

Table 6 has shown the types of operations done under Fluothane anesthesia; table 8 details the length of time for the operations. In a practice such as ours there were necessarily a large number of anesthesias for abdominal operations. As previously stated, we did not attempt to obtain profound relaxation with Fluothane, because in maintaining the concentration sufficient to provide adequate abdominal relaxation in the adult the fall in blood pressure was excessive. We therefore provided the relaxation by using succinylcholine drip. The total amount of muscle relaxant required for relaxation was not excessive. For an exploratory laparotomy of two and three-quarters hours duration in a 50 year old woman, 350 mg. of succinylcholine were required. In a 41 year old woman having an appendectomy requiring one and a quarter hours, 120 mg. of succinylcholine were used for muscle relaxation. Several patients having gastric resections were carried for a time on Fluothane, but the amount of muscle relaxant required seemed too great so it was abandoned and ether used. Gallbladder surgery, however, for the most part could be done with a reasonable amount of muscle relaxant under this anesthesia. In infants and children it was possible to provide adequate relaxation with Fluothane alone without too great a fall in blood pressure.

Of the genitourinary cases the majority were for cystoscopic examinations which required but little more than nitrous oxide, after Pentothal induction. Fluothane was a good adjunct to provide the small amount of additional anesthesia needed. Over 95% of these were awake enough to help themselves off the table and were able to return to their rooms instead of the recovery room. In using the open drop insufflation technic of Fluothane for children having cystoscopy, frequently the child would seem to be sufficiently anesthetized to insert the cystoscope but would move when this was attempted. Deeper anesthesia with Fluothane allowed the urologist to proceed. We found that stimulation of the skin by preparation with ether before operation, or the skin incision often caused the patient to move under light Fluothane anesthesia. The lack of cutaneous anesthesia seems to be one of the peculiarities of Fluothane. We still prefer spinal anesthesia for the transurethral resection in the age group needing such an operation, but some of the younger men had this procedure under Fluothane, nitrous-oxide, and succinylcholine without incident.

Neurosurgical procedures, in which the surgeon almost always demanded the cautery, and which usually do not need muscle relaxation, did well with the small amount of Fluothane necessary to give good operating conditions.

For extra-abdominal surgery such as breast, neck, or extremities, Fluothane is excellent except that it is necessary to have the patient well anesthetized for the skin incision. We have had opportunity to use Fluothane in only 9 open chest operations but found no untoward symptoms in this small series.

For obstetrics, in the not too heavily medicated patient, Fluothane by the open drop technic or by the semiclosed method provided excellent anesthesia without any untoward sequelae. In the heavily sedated patient the recovery time of the delivered woman was

TABLE 8

LENGTH OF SURGERY WITH FLUOTHANE

Less than ½ hr.	537
½ hr. to 1 hr.	591
1 hr. to 2 hrs.	606
2 hrs. to 4 hrs.	238
Over 4 hrs.	28
	2,000

prolonged. As soon as the surgical stimulation was absent the mother would fall asleep again and could only be aroused with painful stimulation. The infants in 82% cried within 30 seconds even in the heavily sedated patients, so in a delivery of normal length, with episiotomy and outlet forceps, we do not believe Fluothane depresses the infant any more than equal anesthesia with any of the other general anesthetic agents. Since this series reports of excessive bleeding postpartum, this has caused us to abandon the use of Fluothane in obstetrics though we had no difficulty in our cases.

We particularly like Fluothane for minor orthopedic procedures on outpatients because it is possible to produce rapid, smooth anesthesia with enough relaxation for bone-setting on the unprepared patient. Usually he quickly and fully regains his reflexes in a few minutes with infrequent nausea and is able to leave the emergency room.

The rapid and complete recovery with infrequent excitement, or nausea and vomiting is one of its outstanding properties. On the last 500 of this series we studied the incidence of nausea and vomiting following Fluothane anesthesia and found that 4% vomited within the first 4 hours and 9% within the first 24 hours. There are many other factors to be considered besides the anesthetic agent in causing postoperative vomiting but our impression was that it was markedly reduced with this agent.

Complications from the administration of Fluothane in this series were few, nor were they serious. In most they were due to faulty technic of administration from inexperience with the drug or from equipment not capable of delivering an accurate percentage of this potent agent. The most common complication was too deep an anesthesia, especially in using the open drop technic in children. Bradycardia occasionally occurred but usually was relieved by intravenous atropine and by reducing the vapor concentration. Like cyclopropane, Fluothane increases cardiac irritability and therefore drugs such as epinephrine should not be used with this agent.

The signs of the level of anesthesia are the same, in general, as with ether, except they occur more quickly. One of the most important single signs is related to respiration; with deepening anesthesia the intercostal muscles are paralyzed and the level of anesthesia can be followed accurately by the character of respiration. Consciousness disappears with the establishment of Level I. The eyelid reflex also is lost in Level I. Oscillation of the eyeball usually is abolished in Level II but often in Level I. Pupils remain constricted until deep levels when they dilate. Lacrimation remains until Level II. Spontaneous apnea similar to cyclopropane apnea occurs at Level IV. Progressive paralysis of the intercostal muscles occurs but sometimes too rapidly to be appreciated. Controlled respiration is easy at any level. It is not unusual for the rate of respiration to be 28 to 30 throughout, and the amplitude somewhat depressed. The jaw relaxes profoundly, in fact, it is so complete that insertion of an oral airway is frequently required to maintain a completely unobstructed airway. Intubation can be done under Fluothane without a muscle relaxant provided the operator requires but one try, since the recovery time is so rapid that after one try the patient is almost awake. There seems to be considerable obtunding of the pharyngeal and laryngeal reflexes with less "bucking" on the endotracheal tube even under light anesthesia.

Comments

This study with Fluothane was not done at a university center. None of the administrations of the anesthetic were done by internes or residents, but were given by well qualified and experienced anesthetists. As may be seen from the age distribution, over half of the patients were between 21 and 50 years of age (Table 5). There were very few poor risk patients in this group. The length of operation in two-thirds of the cases was less than two hours (Table 7). We believe a machine with an accurately calibrated vaporizer is essential to the safe and proper use of this potent agent. It should be noted that over half of the anesthesias in this series were given with the Copper Kettle, probably one of the most accurate vaporizers on the market. The figures in this study are accurate, though it might be difficult to duplicate them without the ideal conditions just listed. We were a little surprised, for example, to find that four-fifths of the patients in this series were awake or awake enough to open their eyes on request within 3 to 5 minutes after the operation. Considering that the Fluothane was turned

off or markedly decreased 5 to 10 minutes before the end of the operation, and that maintenance was kept on 0.60 to 1.0% of Fluothane vapor plus the factors just listed above, the recovery time is not so unusual.

Due to the ease with which one can administer a lethal concentration of this agent, it is our belief that this drug is suitable for use in a machine with an extremely accurate vaporizer. Used by the open drop technic or by any method, the anesthetist must be alert and should be experienced. This is not a drug for the "occasional anesthetist" or the unsupervised student of anesthesia. Properly used it is one of the most useful anesthetic agents to date.

Advantages

1. Nonirritating to respiratory tract.
2. It inhibits salivary and bronchial secretions.
3. Not unpleasant to inhale.
4. Rapid induction, rapid recovery.
5. Nonexplosive.
6. Potent.
7. Can be used with soda lime.
8. Diminished bleeding without extreme hypotension.
9. Can be used as a reversible hypotensive agent.
10. Controlled respiration is easy.
11. Less postoperative vomiting.
12. Low incidence of post hypotension and shock.

Disadvantages

1. May cause arrhythmias.
2. Moderate relaxation.
3. Incompatible with epinephrine.
4. Respiratory depressant.
5. Cardiovascular depressant.
6. Not for unskilled anesthetist.
7. Potent.

Summary

A nonexplosive volatile anesthetic drug has been used as the principal agent in 2,000 unselected anesthetics in patients of all ages from 5 weeks to 82 years with the commonly used technics. We believe that there is a distinct need for a controlled volatile nonexplosive anesthetic agent, and it is quite possible that this halogenated ethane is of more than passing interest in filling the need. After using it in this series we were impressed with the rapid smooth induction, the ease of maintenance with present anesthesia equipment, the reduction of salivation, the rapid reversibility of its action by controlling the vapor concentration, the adequate muscular relaxation for most procedures, the rapid recovery time without excitement, the reduction in nausea and vomiting, and the minimal complications. We believe it has already made a place for itself with the anesthesiologist but, of course, deserves further study.

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Fluothane: Incidence and Significance of Hypotension*

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The hypotensive effect of Fluothane is considered as well as the means to combat or avoid this.

A NEW FLUORINATED ETHANE COMPOUND, Fluothane (trifluro-chlorobromo-ethane) or Halothane, has been in use in Great Britain since 1955[1] and in this country since 1956.[2] Its principal advantages include nonflammability, ease and smoothness of induction, absence of secretions, early obtundation of pharyngeal and laryngeal reflexes, rapid elimination from the body and low incidence of nausea and vomiting. At the same time Fluothane is remarkably potent. Induction concentrations vary from 1.5 to 2.5 volumes per cent and maintenance concentrations range from 0.6 to 1.5 volumes per cent. In the search for the perfect anesthetic agent, Fluothane seems to possess some of the required qualities. Its nonflammability in oxygen makes possible the safe use of all electrical appliances in the operating room and might eventually make unnecessary the elaborate precautions taken to prevent fires and explosions. In the opinion of most authors it provides satisfactory muscular relaxation for all procedures, with the possible exception of surgery in the upper abdomen.

Potential drawbacks have been found. Occasional struggling during the excitement stage may occur; the delayed appearance of a total analgesic effect has been noted. These limitations are of minor importance.

Of greater significance is the knowledge that the intravenous injection of epinephrine in the dog anesthetized with Fluothane precipitates ventricular fibrillation. At the same time, when administered subcutaneously to the animal, epinephrine can be injected in large doses and in high concentrations without the appearance of significant arrhythmias.[3] However, species differences are important and the subcutaneous administration of epinephrine to patients under Fluothane anesthesia has not been investigated thoroughly. Due to the extreme variations of tolerance of human subjects to epinephrine, its clinical use in association with Fluothane anesthesia remains a potential hazard.

Muscle relaxant drugs should be used with discrimination during Fluothane anesthesia. D-tubocurarine chloride has been shown to cause a severe circulatory depression and is best avoided. Gallamine triethodide must be used in reduced dosage and its effect may be expected to last considerably longer than when used with other anesthetic agents.[4] However, succinylcholine chloride will provide the anticipated effect with a normal dosage and the usual technics.

Of perhaps greatest practical significance is the fall in blood pressure which may be associated with the induction of Fluothane anesthesia. This hypotensive effect was mentioned in the early reports and has been confirmed subsequently by all clinical investigators. In a series of 1,500 cases in this clinic[5] the incidence of fall of blood pressure greater than 20 mm. Hg. systolic was 35% during the induction of anesthesia. However, only 12% of patients developed significant variations of pressure during maintenance of anesthesia. The incidence and degree of hypotension appears to be directly proportional to the concentration of the drug to which the patient is exposed. Since higher concentrations are required during induction, the

TABLE 1

THE DIFFERENT ANESTHETIC COMBINATIONS USED IN THE CONTROL SERIES

Surital sodium, nitrous oxide, and succinylcholine	6
Surital sodium, nitrous oxide, meperidine and succinylcholine	33
Surital sodium, nitrous oxide, ether and succinylcholine	37
Surital sodium, nitrous oxide, cyclopropane and succinylcholine	24

*Read before the Section on Anesthesiology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

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TABLE 2

AGES OF THE PATIENTS IN BOTH SERIES OF CASES

Age in Years	*Fluothane*	*Other Agents*
Less than 10	2	1
" " 20	10	8
" " 30	15	19
" " 40	25	23
" " 50	27	24
" " 60	17	15
" " 70	3	9
More " 70	3	1

incidence of hypotension is greater during this phase of anesthesia. In almost all instances the blood pressure returns to normal levels once the concentration of drug required for maintenance has been established and usually before the operation is begun.

Clinical Studies

In order to evaluate clinically the incidence and severity of the fall in blood pressure under Fluothane anesthesia, two series of 100 cases each were studied. In the first group Fluothane was the main anesthetic agent. In the control series conventional anesthetic agents were used (Table 1). A similar study has already been reported,[6] involving all types of surgical operations. In order to standardize anesthetic and surgical factors as much as possible, the cases chosen in this series were limited to thoracic operations. In all these patients endotracheal intubation was performed, the patient was turned from the supine to the lateral position, and the operation was a lengthy one accompanied by moderate blood loss and similar types of traction reflexes. Table 2 shows that the range of age was similar in both series, as was the duration of anesthesia (Table 3). Table 4 indicates the type of surgical operations done in both groups. Fluothane was avoided in mitral valvulotomies because of the low cardiac reserve in these patients and the unknown mechanisms of action of Fluothane on the cardiovascular system.

Induction. (Table 5) Fifty-nine patients

TABLE 3

DURATION OF ANESTHESIA IN BOTH SERIES OF CASES

Duration in Hours	*Fluothane*	*Other Agents*
Less than 1	1	
" " 2	4	5
" " 3	24	21
" " 4	38	28
More " 4	33	46

TABLE 4

TYPES OF OPERATION IN BOTH SERIES OF CASES

Operation	*Fluothane*	*Others*
Exploratory thoracotomy	12	20
Excision of coin lesion	2	2
Segmental or wedge resection	41	17
Lobectomy	21	23
Lobectomy and segmental resection	4	4
Excision of blebs or cysts	3	3
Decortication of the lung	3	1
Thoracoplasty		1
Pneumonectomy	3	1
Hiatus hernia repair	2	1
Esophageal diverticulum		1
Esophago-gastrectomy		3
Esophageal stricture		2
Mediastinal tumors	3	
Thymectomy	1	3
Splanchnicectomy with celiac gangliectomy		2
Excision of pericardium	2	1
Mitral valvulotomy		11
Ligation of patent ductus	2	2
Coarctation of aorta		1
Cancelled before surgery	1	1

anesthetized with Fluothane exhibited a fall in blood pressure during induction. Only 31 of those anesthetized with other agents showed a similar hypotension. However, in the Fluothane patients, only 10% of the 59 had a fall in blood pressure of greater than 40 mm. of Hg. systolic. In the control group, similarly, 10% of the 31 patients had a fall greater than 40 mm. of Hg.

Change in Position. (Table 6) Fifty-six patients under Fluothane and 40 patients anesthetized with other agents had a fall in pressure when their position on the table was changed. Again there was a greater incidence with Fluothane than with the other agents. However, the fall in blood pressure in the Fluothane group was not considered of great significance because in 48 of the 56 patients the drop was less than 30 mm. Hg. systolic.

Maintenance. (Table 7) During operation a fall in blood pressure occurred in ap-

TABLE 5

INCIDENCE AND DEGREE OF HYPOTENSION DURING INDUCTION

mm. of Mercury	*Fluothane*	*Other Agents*
More than 20	27	11
" " 30	20	8
" " 40	6	7
" " 50	1	3
" " 60	3	
" " 70		1
" " 80	2	1
Total	59	31

TABLE 6

INCIDENCE AND DEGREE OF HYPOTENSION ASSOCIATED WITH THE CHANGE IN POSITION

mm. of Mercury	*Fluothane*	*Other Agents*
More than 10	31	23
" " 20	17	11
" " 30	4	2
" " 40	2	3
" " 50		
" " 60		
" " 70		
" " 80	2	1
Total	56	40

proximately an equal number of cases in both groups. The degree of hypotension also was almost identical. In most instances this fall in blood pressure could be attributed to extraneous factors, such as blood loss or traction reflexes on the hilum. The use of Fluothane did not appear to predispose patients unduly to development of hypotension during operation.

Discussion

The mechanism of the fall in blood pressure which occurs under Fluothane has not been elucidated completely. Several suggestions have been made.

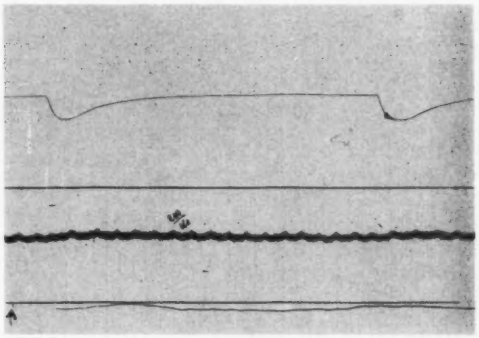
(1) Raventos[7] has attributed the hypotension to a ganglionic blocking effect which produces a peripheral vasodilatation. After noting some diminution of the response of the nictitating membrane of the cat, he states that "there is some specificity in the action of Fluothane on different ganglia . . . and it seems likely that the mesenteric ganglion is more sensitive to its action than the superior cervical ganglion." The significance of the peripheral vasodilatation as a cause of hypotension has been disputed by a research group in England.[8] They report that deep planes of Fluothane anesthesia do not produce a ganglionic blocking effect.

TABLE 7

INCIDENCE AND DEGREE OF HYPOTENSION DURING OPERATION

mm. of Mercury	*Fluothane*	*Other Agents*
More than 20	25	22
" " 30	17	17
" " 40	10	8
" " 50	3	3
" " 60	2	1
" " 70		
" " 80	2	4
Total	59	55

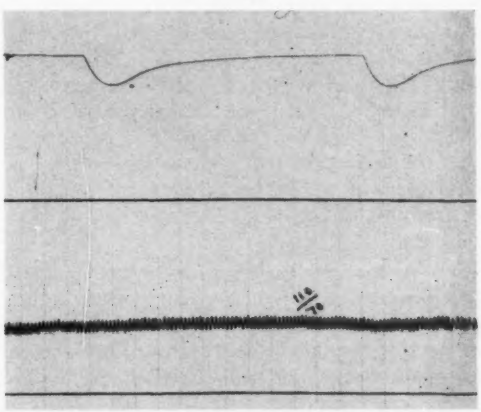
FIG. 1



Contraction of the nictitating membrane on the "control" cat after stimulation of the preganglionic sympathetic fibers. The B.P. is 200/160.

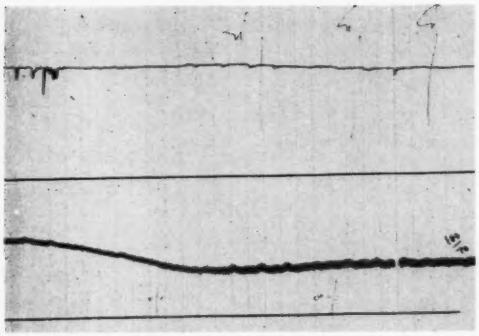
A type of experiment similar to that of Raventos has been performed by us. In 6 cats the cervical sympathetic chain was dissected out and prepared for electrical stimulation. The nictitating membrane of the animal's eye was attached to the rubber membrane of a drum by fine black silk. The drum itself was connected by copper tubing to a fine sensitivity (0.05 psi) Statham transducer so that variations in pressure within the drum, caused by movements of the nictitating membrane, could be recorded on a Grass machine. "Control" stimulation of preganglionic fibers elicited, through transfer across the superior cervical ganglion, a contraction of the nictitating membrane (Fig. 1). The animals were then anesthetized with Fluothane to plane 3, stage 3, as indicated by marked intercostal

FIG. 2



Contraction of the nictitating membrane of the same cat under deep Fluothane anesthesia. The B.P. is 110/70.

FIG. 3



After elimination of the Fluothane, a 0.1% drip of Arfonad has lowered the B.P. to 100/70. No contraction of the nictitating membrane can be elicited.

paralysis. A pronounced fall in blood pressure accompanied the intercostal paralysis. The electrical stimulation of the sympathetic fibers was repeated and in each instance a contraction of the nictitating membrane was elicited (Fig. 2). The amplitude of this contraction was almost as great as in the control animals. In 3 animals the Fluothane was eliminated and then Arfonad, 0.1%, was administered by intravenous drip until the blood pressure reached a level similar to that obtained under Fluothane. Electrical stimulation of the preganglionic sympathetic fibers was repeated. In each animal no contraction of the nictitating membrane was elicited (Fig. 3). This experiment appeared to indicate that Fluothane did not have any significant ganglionic blocking action on the superior cervical ganglion of the cat.

(2) A direct myocardial depressant effect has been suggested as the cause of hypotension under Fluothane anesthesia. Burn and his associates[8] in England used the dog heart-lung preparation and emphasized the fact that Fluothane has some depressant effect on the myocardium of the dog. At a concentration of less than 1.2% however, which is equivalent to maintenance concentration, the depressant effect on the myocardium is negligible.

(3) A further explanation of the fall in blood pressure lies in a possible central depression of the vasomotor center. It has been suggested, on the basis of depression of the knee-jerk reflex in the cat, that the hypotension may be on a central basis.[8]

(4) One other mechanism which has not been investigated for Fluothane may be suggested. Robertson and Swan[9] found, in a series of experiments, that stimulation of the baroreceptors by clinical concentrations of ether and chloroform resulted in marked drops in blood pressure in the experimental animal. Fluothane might act in a similar manner.

From the practical viewpoint, if the cause or causes of the fall in blood pressure could be defined accurately, steps might be taken to avoid or prevent them. In the anesthetized patient hypotension in the absence of hemorrhage usually can be ascribed to peripheral vasodilatation, myocardial depression with decreased cardiac output, or to reflex phenomena acting indirectly either peripherally or centrally.

Observation of patients under Fluothane anesthesia shows consistently warm, dry, pink extremities, with full, bounding peripheral pulses and marked venular dilatation. The appearance is similar to the peripheral vasodilatation seen following administration of ganglionic-blocking drugs or chlorpromazine. However, laboratory data, as noted above, make it unlikely that the hypotension can be explained on the basis of a ganglionic blockade. A direct effect on the vasomotor center could explain the clinical appearance, but there are no data to support this belief at the present time.

The venular dilatation could result from pooling of blood on the venous side of the body and could be due to decreased cardiac output. Evidence is mounting that Fluothane does produce direct myocardial depression in concentrations greater than 1.2 per cent.[8] Such concentrations are required during the induction of anesthesia, but seldom during maintenance. The best evidence at present indicates that a direct myocardial depression will explain the hypotension seen during induction. With the lesser concentrations required for maintenance, the effect on the heart is reduced and blood pressure returns toward normal (Fig. 4).

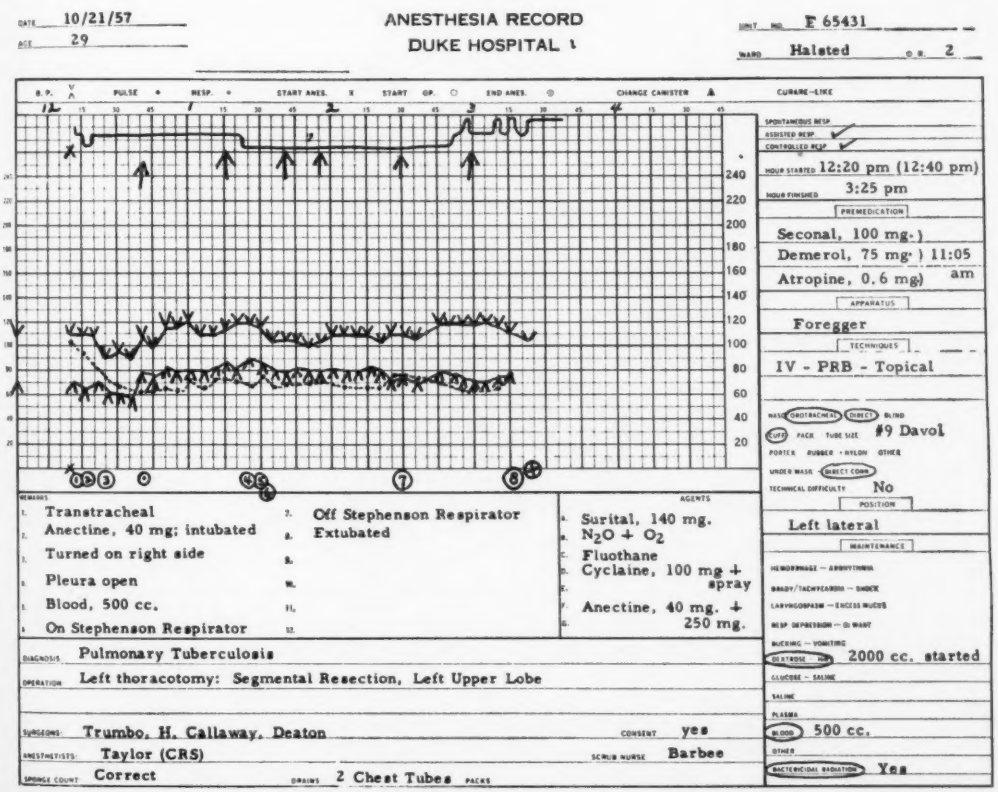
The possibility of reflex stimuli being responsible for the hypotension cannot be eliminated. Fluothane does cause an increase in vagal tone and, if this effect is marked, bradycardia and hypotension will ensue. Normotension can be restored by administration of an anticholinergic drug.

It has become apparent that the degree of hypotension seen with Fluothane is related to the depth of anesthesia, which in turn is dependent on the concentration of Fluothane in the inhaled mixture. Bitter experience has led us to realize that safety in administration of Fluothane is enhanced by proper and accurate means of vaporization. The classical signs of anesthesia appear so rapidly that control of the depth of anesthesia by clinical observation alone is most difficult. Since the onset of hypotension can be controlled to some extent by limiting concentrations inhaled, it follows that this complication can be minimized by accurate vaporization.

For safe administration of Fluothane, vaporizers are required which will deliver concentrations between 0 and 3.5% and which are calibrated for different flows of gases. Furthermore, these vaporizers should permit one to alter the concentration in tenths of 1.0% and should be so placed in the anesthetic circuit that the flow of gas through the vaporizer is known at all times.

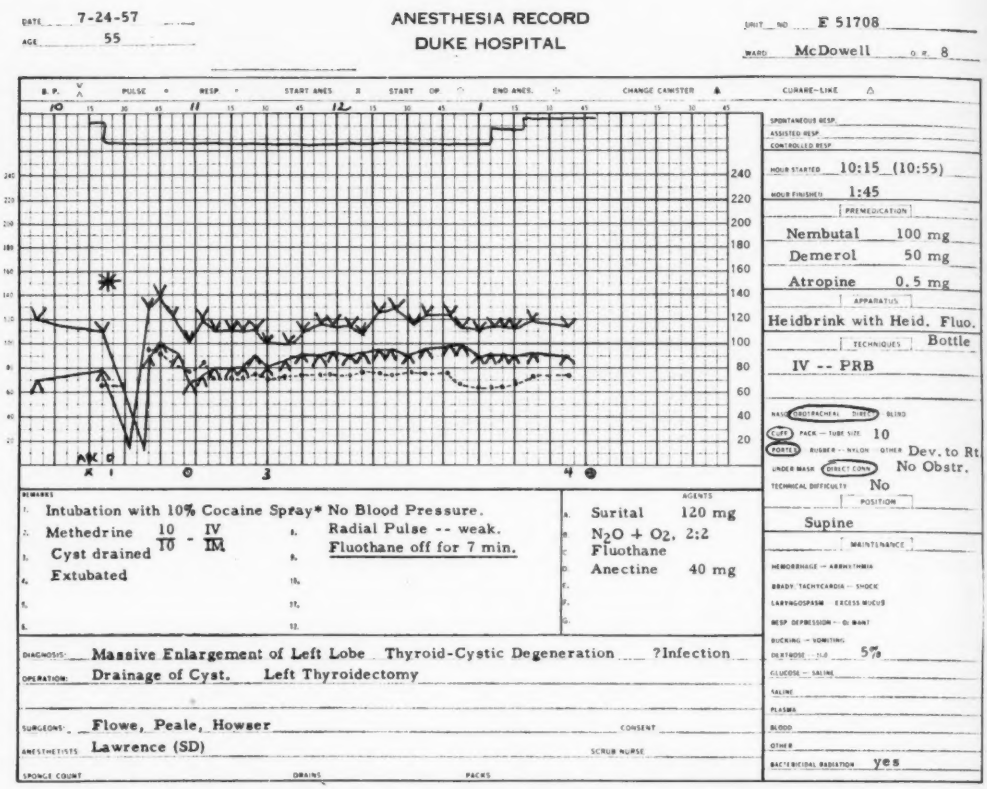
The use of Fluothane in a closed system can lead to a rapid build-up of high concentrations of the drug. When the Fluothane vapors are diluted in a flow of 4 to 6 liters of gas, it is easier to provide a fine and more flexible control of the concentration of the vapor. This results in a safer administration. If a closed system is to be used the location of the vaporizer in the circuit is of considerable importance. It must be placed between the gases being supplied from the machine and the inlet to the circle system. If the vaporizer is incorporated within the circle filter or head of the machine itself, the concentration of Fluothane will vary with the minute volume of the respiration and conse-

FIG. 4



Anesthetic record of a patient who had a thoracotomy under Fluothane anesthesia. A fall in B.P. of 20 mm. systolic is noted during induction. At the time of incision the B.P. is back to normal.

FIG. 5



An example of severe cardiovascular depression which occurred under Fluothane. In this case, the Fluothane vaporizer was incorporated in the circle system. The cardiovascular collapse occurred when the minute volume of the patient was suddenly increased which resulted in the patient receiving a high concentration of Fluothane.

quently will not be known accurately. Under these circumstances, if the respiration is assisted or controlled, dangerously high concentrations may be administered and can result in severe cardiovascular accidents[5,10,11] (Fig. 5).

Summary

It has been found that during the induction of anesthesia greater drops in blood pressure occur with Fluothane than with other anesthetic combinations. The fall in blood pressure appears to be a direct reflection of the concentration of Fluothane to which the patient is exposed. Safe administration of Fluothane implies accurate means of vaporization within the clinical ranges of usefulness. Such accurate concentrations can be provided only with vaporizers specially calibrated for Fluothane which are so placed in the circuit that the flow of gases passing over them is known at all times.[12]

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Discussion (Abstract)

Dr. Howard M. Ausherman, Charlotte, N. C. There is a distinct need for a nonexplosive anesthetic agent with potency sufficient to provide adequate relaxation for most operative procedures. Fluothane, a halogenated ethane, seems to fulfill this requirement. Though it has been in the hands of research workers less than two years, approximately 20,000 administrations have been carried out in humans. Several pieces of knowledge have been found, one of these, the fall in blood pressure, is the topic of the excellent paper you have just heard. As pointed out by Dr. Bourgeois the fall may be explained by several theories. The fact is, however, that by whatever means it occurs, the most marked drop is during induction when the concentration of Fluothane is the highest. The blood pressure fall during induction with Fluothane is greater than with other agents and is about equal to that produced by other agents during maintenance. Since Fluothane seems to be an excellent agent when properly administered, the problem lies in providing an accurate method of delivering a finely calibrated vapor to avoid high concentrations and accompanying drop in blood pressure, obtaining relaxation not by the depth of anesthesia but by a muscle relaxant such as succinylcholine.

This is successfully accomplished by induction with another anesthetic agent or slowly and gradually introducing Fluothane into the system by means of a finely and accurately calibrated vapor.

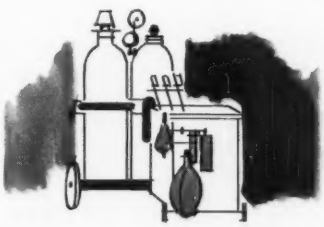
Safety in the administration of Fluothane lies in accurate vaporization. First, by using a means of vaporization already on the market (the Copper Kettle of Foregger) graduations in tenths of 1% can be delivered. Secondly, by using a semiclosed technic, with a flow of 4 to 6 liters, it is easier to avoid building up the high concentrations that might result from a closed technic. Thirdly, the vaporizer should be placed *between* the gases supplied from the machine and the inlet to the absorption system.

If the vaporizer is incorporated in the absorption system the concentration of Fluothane will vary with the minute volume of respiration, hence will not be known accurately. With assisted or controlled respiration dangerously high concentrations may be given.

We have found that actually the drop in blood pressure from Fluothane in our series of over 1,000 administrations can be kept to a negligible minimum by this simple means.

Finally, Fluothane, due to its potency, is no drug for the "occasional anesthetist." It requires skill and judgment in its use and properly calibrated equipment graduated in tenths of 1% for its safe use.

It will, I believe, find a place in the armamentarium of the anesthesiologist if these important precautions are carried out in its use.



Adenomatoid Tumors of the Epididymis: Report of Three Cases with Histochemical Studies and Review of Literature

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This extensive review brings the subject up to date. By histochemical staining methods the author adds a new contribution to the knowledge of the etiology of such tumors.

THE PURPOSES OF THIS PAPER are to present new histochemical aspects of adenomatoid tumors of the epididymis that affect interpretations of the origin of these tumors, to report three additional cases of adenomatoid tumor of the epididymis, to summarize all accepted instances of these tumors previously reported, and to make a plea for the conservative treatment of these tumors.

Increasing numbers of primary tumors of the epididymis (Table 1) are now being recognized and reported although such tumors were once thought a rarity.[1,2] Adenomatoid tumors comprise the bulk of benign epididymal tumors,[3] and it is clear that benign tumors of the epididymis vastly outnumber the primary malignant neoplasms of this organ.[4,5] Adenomatoid tumors are solid neoplasms of a benign nature peculiar to the genital tracts of both the male and female, and characterized by a distinctive adenomatous microscopic appearance.

Histochemical Study

Theories of Origin. A great deal of controversy exists as to the etiology of adenomatoid tumors, leading in the widespread confusion in diagnostic terminology. The major theories embrace mesothelial, endothelial, epithelial, or mesonephric tissue as the site of origin of these unique tumors.

Most widely accepted is the theory of mesothelial origin,[6-8] and the anatomic proximity of these tumors to mesothelium of tunics and peritoneum lends weight to this theory. This hypothesis assumes that adenomatoid tumors are derived from the multipotential mesothelium of the urogenital ridge. Also, the similarity of adenomatoid tumors to pleural and peritoneal mesotheliomas has been pointed out. However, the histochemical studies of this report reveal certain striking differences between adenomatoid tumors and mesotheliomas.

The endothelial theory of origin is based upon the belief that the adenomatous spaces of the tumor are lined by flat endothelial cells, and the strands and cords of cuboidal cells are regarded as the result of metaplasia.[9,10] However, the spaces do not contain hematogenous or lymphogenous elements. Further, the lining cells appear to be typical tumor cells which have been flattened by the enlarging spaces.[11]

Exponents of the epithelial theory of origin have suggested that adenomatoid tumors arise as a transition from normal epididymis.[12] Vacuolization of the neoplastic cells has also been offered as evidence of epithelial origin. Origin of the tumor in the epithelial rem-

TABLE 1

CLASSIFICATION OF PRIMARY EPIDIDYMAL TUMORS

Benign Tumors—comprising approximately 75% of epididymal tumors
1. Epithelial—one reported, unless theory of müllerian or wolffian vestige is accepted
2. Mesothelial—including lipoma, fibroma, myxoma, leiomyoma, cholesteatoma
3. Endothelial—lymphangioma, angioma
4. Heterologous—cystic dermoid, cystic embryoma
5. Adenomatoid—a neutral classification, avoiding the conflict of theory of origin and comprising 50% of all epididymal tumors

Malignant Tumors—25% of primary epididymal tumors
1. Epithelial—carcinoma
2. Mesothelial—sarcoma
3. Heterologous—teratoma

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nants[13] of the wolffian system or müllerian duct is not probable since adenomatoid tumors in women do not show the cyclic changes expected of müllerian derivatives nor are the tumors found in the region of wolffian remnants.[14] A similarity of adenomatoid tumors to cystic papillary carcinoma is apparently only superficial.[15] Finally, the suggestion that the mesonephros gives rise to adenomatoid tumors[16] and that these tumors may actually represent hamartomas of the mesonephros[3] remains unsupported.

For the present, the question of origin must remain open, and the "descriptive and noncommittal" diagnostic term "adenomatoid tumor" should be employed.[11] While the mesothelial theory of origin remains the most acceptable, histochemical analyses emphasize certain distinct differences between adenomatoid tumors and mesotheliomas. These striking differences have not been reported previously, and are outlined in detail below.

Pathologic anatomy and classification. Grossly, adenomatoid tumors of the epididymis average 2 cm. in size with extremes of 0.5 cm.[17] to 45 cm.[18] reported. The tumors are firm, rounded, smooth and usually loosely encapsulated. The appearance is quite similar to fibromyoma uteri. Consistency is rubbery, and the cut surface bulges and shows a sworl like arrangement of fibrous tissue. The color is grayish-white and glistening with yellow flecks.

A classification of epididymal tumors is presented in table 1.

The histologic picture of adenomatoid tumors varies slightly depending upon the relative amounts of fibromuscular, adenomatoid, and sclerotic components in any individual tumor.[19] Three major histologic patterns are seen: a canalicular arrangement simulating vascular spaces, a tubular pattern with gland-like spaces, and a plexiform architecture of strands and nests of cells.[20] The cells have an homogenous eosinophilic cytoplasm with occasional vacuoles of varying size. Nuclei are uniform and strongly basophilic with well defined nuclear membranes and prominent central nucleoli. The channels or spaces are lined by flattened endothelial-like cells, and while previous reports indicate that these spaces are empty, study of the three tumors reported here reveals frequent desquamated cells and amorphous debris. The development of the adenomatoid spaces may be traced from vacuole formation through coalescence of the vacuoles with subsequent compression of surrounding cords.[11] Fibrous stroma varies in amount and usually contains bundles of smooth muscle, focal collections of lymphocyte, and occasional plasma cells and polymorphonuclear leukocytes. Often lymphoid nodules are found. The pseudocapsule of the tumor is composed of compressed collagenous tissue. Mitoses are rare and there is no cellular variation to suggest malignancy. Invasion is not seen though regions of transition may give a false impression of invasion.

Comparison. Comparison of the adenomatoid tumors of this series with the histologic picture of a pleural mesothelioma and a peritoneal mesothelioma, both specimens obtained at autopsy, shows a marked superficial similarity in architecture. This similarity undoubtedly accounts for a great deal of the support given the diagnosis "mesothelioma of the epididymis." However, the peritoneal mesothelioma particularly revealed a high degree of anaplasticity not evident in the tumors of the epididymis. There was no similarity between the adenomatoid tumors and an adrenal rest tumor of the epididymis examined.

Histochemical studies. Stains employed in this study included the periodic-acid-Schiff using McManus' method,[21] Pearse's method for Sudan Black B,[22] mucicarmine,[23] Sudan IV,[24] and Best's carmine method for glycogen.[24] Similar preparations were made of all three adenomatoid tumors and of known mesotheliomata.

Sudan IV fat stains of the adenomatoid tumors of the epididymis show finely dispersed granules of neutral fat present in faint quantities in the cells of the cords and strands of the tumors. Glycogen stains are negative. Periodic-acid-Schiff stains reveal granular deposits of Schiff-positive material within the cytoplasm of desquamated cells and lining cells as well as within the vacuoles of other tumor cells. Mucicarmine stains are positive for mucin within the vacuoles of cells of the adenomatoid tumors. A Sudan Black preparation in each instance demonstrates the presence of formalin-fixed lipids in a majority of

the tumor cells, lying in small vacuoles and perinuclear mitochondrial areas.

These histochemical findings in adenomatoid tumors of the epididymis have not been elaborated previously, and are significant in establishing aspects of the metabolism of these tumors which deserve further study. Similar histochemical studies of pleural and peritoneal mesotheliomas did not reveal the presence of neutral fats, glycoproteins, phospholipids, mucopolysaccharides or mucin as was demonstrated in the adenomatoid tumors of the epididymis.

Thus the metabolism of adenomatoid tumors of the epididymis apparently differs from that of other mesothelial tumors, though the histologic picture and gross location indicate a probable mesothelial origin of adenomatoid tumors. If this is the case, then two possibilities must be considered: either the difference in growth potential between adenomatoid tumors and mesotheliomas accounts for the differences in cellular metabolism, or adenomatoid tumors are of an entirely different etiology than mesotheliomas. Recent reports of adenomatoid tumors in the newborn and of many years duration stimulate speculation as to a possible congenital origin; adenomatoid tumors might be simply congenital malformations of mesothelial tissue. While data gained from this study has not demonstrated this etiology, histochemical investigation opens new avenues of approach to the problem.[25-28]

FIG. 1

(Case 1) Gross specimen. The firm, white tumor mass is seen lying below the testis within the hydrocele sac. The epididymis has been largely obliterated. Cases 2 and 3 were similar.

FIG. 2

Typical microscopic appearance of adenomatoid tumor with characteristic spaces lined by flattened cells. Interposed strands of tumor cells are quite regular in appearance. (X 100).

Case Reports

Case 1. J. H., a 64 year old colored man, admitted for treatment of hypertensive cardiovascular disease, gave a history of a mass in the left scrotum, present and gradually enlarging over the preceding 12 to 13 years. Examination revealed a mass 10 by 5 by 5 cm. occupying the left scrotal compartment. The mass was semicystic at its upper pole and extremely firm at its lower pole. It did not transilluminate. A left inguinal orchiectomy was performed with a preoperative diagnosis of testicular tumor. The postoperative course was uneventful. The patient was seen 3 months later and was doing well without evidence of recurrence.

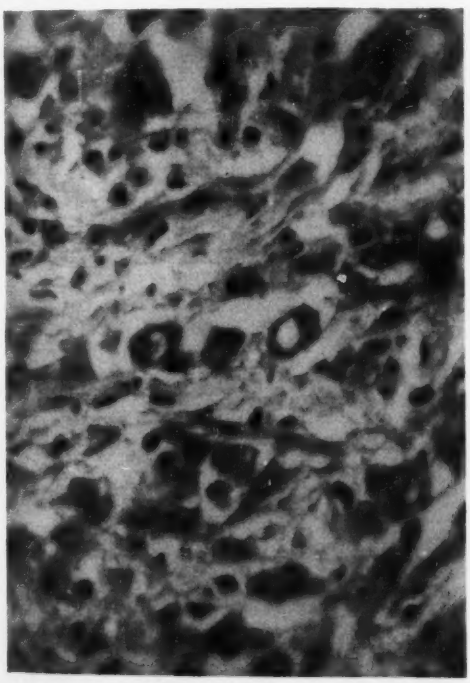
The gross specimen was the left testis, epididymis, tumor, and 6 cm. of the cord with a small hydrocele containing clear, straw-colored fluid (Fig. 1). The tumor measured 3 by 3 by 4 cm. It was stony hard and was attached to the lower pole of the epididymis. On cut section, the tumor was fibrous, bulging and

grayish-white with yellow flecks. The histologic picture was typical of adenomatoid tumor of the epididymis (Fig. 2). Homogenous acidophilic cells with uniform nuclei were arranged in regular strands, cords, and adenomatoid spaces lined by flattened cells. Some vacuolated cells were present. Masson and Van Geison stains demonstrated the presence of fibrous and smooth muscle tissue, predominantly in the pesudocapsule of the tumor. Focal collections of lymphocytes were present.

Histochemical study included a mucicarmine stain which was positive for small quantities of mucin within the adenomatoid spaces and with the vacuoles of many cells (Fig. 3). Periodic-acid-Schiff stain revealed Schiff-positive material within desquamated cells lying in the spaces, and Schiff-positive material was also present in the cellular vacuoles. A Sudan Black stain confirmed the presence of phospholipids in the tumor cells, most conspicuously in the cells lining the spaces and lying within the spaces. The Sudan IV preparation showed finely dispersed granules of fat in many of the tumor cells.

Case 2. J. J., a 37 year old white married man, was admitted elsewhere for removal of a testicular tumor. The patient had suffered trauma to the scrotum 15 years previously, and had noticed a painless mass, gradually enlarging, in the region of the left testis 10 years prior to admission. In the week before admission, there had been some soreness in the region of the mass. The patient was found to have a diffusely tender swelling about the size of a walnut at the lower aspect of the left testis. Left inguinal orchiectomy was done, and the specimen was submitted to this laboratory for examination. The postoperative course was uneventful, and the patient's course was followed for 3 years without recurrence of the tumor. He died of a ruptured cerebral aneurysm.

FIG. 3



Mucicarmine preparation showing two typical vacuolated cells at the center. Mucicarmine-positive material is seen within one vacuole and lining the other vacuole. Periodic-acid-Schiff preparations were similar. (X 610).

Grossly, the tumor was a rounded firm mass 2 cm. in size at the tail of the epididymis. The portion of the cord submitted included a hydrocele containing about 25 cc. of fluid. The testis appeared normal. The microscopic picture was similar to that described in the previous case. The tumor arose from the lower pole of the epididymis, was well-encapsulated, and showed no tendency to invade surrounding structures. Histochemical studies were identical with those reported in case 1.

Case 3. N. D., a 71 year old white married man, was admitted with a chief complaint of progressive difficulty in micturition of 6 months duration, and an accessory complaint of a mass in the left scrotum since "young manhood," some 40 to 50 years. Examination revealed extensive carcinoma of the prostate by rectal examination, and a firm nodule 1 cm. in diameter at the upper pole of the left epididymis. Laboratory and x-ray findings corroborated a diagnosis of carcinoma of the prostate, and bilateral epididymo-orchiectomy was performed. The postoperative course was smooth, and the patient expired 3 years later with extensive metastatic carcinoma of the prostate, without evidence of recurrent epididymal tumor.

The gross specimen consisted of both testes, epididymes, and cords, with a firm 1 cm. sized nodule arising in the upper pole of the left epididymis. The tumor was grayish-white and homogenous on cut section, and was covered by a thick fibrous capsule. The microscopic character was typical of adenomatoid tumor. Histochemical studies were identical with those of cases 1 and 2.

Analysis and Discussion

Incidence. Because of the confusion surrounding the exact origin of adenomatoid tumors, they have been variously reported in the literature under diagnoses of angioma,[14] lymphangioma,[29] adenoma,[30] adenocarcinoma,[2] lymphangioepithelioma,[31] epididymomyoma,[32] adenofibromyoma,[33] adenomyoma,[34] "mixed tumor,"[35] fibromyoma,[36] fibroma,[37] leiomyoma,[38] angiosarcoma,[39] and, notably, mesothelioma.[6] The latter term is strongly supported by some writers[7] and is encountered almost as frequently as the term adenomatoid tumor. The use of so many terms makes a precise study of the incidence of adenomatoid tumors difficult.

In the male genital tract, only the testicular tunics give rise to fewer primary neo-

TABLE 2

ADENOMATOID TUMORS OF EPIDIDYMIS REPORTED IN THE LITERATURE

Author	*Year*	*Case*	*History*	*Size (Cm.)*	*Location*	*Diagnosis*	*Treatment*	*Miscellaneous*
Conforti	1910	23	5 mos.	3x6.5	Left	Lymphangio-epithelioma		
Lardennois and Legene	1911	33	"yrs"	1.0	Right	Fibroma		
Naegeli	1912	59			Right	Mischtumor		At autopsy
Sakaguchi	1916	32		2x1.5		Adenomyoma		In epididymis
Stout	1917	57		1	Left	Fibromyoma	Excision	CA bile duct also
Eisenstadt	1923	65	2 yrs.	4.5	Left	Fibromyoma	Orchiectomy	Hydrocele
Hinman and Gibson	1923	78	11 mos.		Left	Adenocarcinoma	Epididymectomy	8 mos.; doing well
Rigganno-Irrera	1925	47		3	Left	Lymphangioma		Lues 4 yrs. before
Rubaschow	1927	23	5 yrs.		Left	Lymphangioma		
Marcandier and Thomas	1930	41				Lymphangioma		
Oberndorfer	1931			Walnut	Right, tail	Lymphangioma	Excision	
Fischer	1932	60	6 yrs.	1.5	Left	Myoadenofibroma		
Mark	1935							Per Golden and Ash
Spivack	1935	46WM	10 yrs.	3x2.5	Right, tail	Leiomyoma	Enucleation	Painful, growing
Thompson	1936	29		1	Right, tail	Adenocarcinoma	Orchiectomy	15 yrs.; doing well
Thompson	1936	54	4 yrs.	1	Right, tail	Adenocarcinoma	Orchiectomy and x-ray	6 mos.; doing well
Thompson	1936	56	15 yrs.	0.7	Left, tail	Adenocarcinoma	Excision	20 yrs.; doing well
Thompson	1936	27	7 yrs.	2.5	Left, tail	Adenocarcinoma	Excision	18 yrs.; doing well
Thompson	1936	30	10 yrs.	2	Left, tail	Adenocarcinoma	Excision	
Scalfi	1936	44		Walnut	Left, tail	Lymphangioma simplex		
Baillie	1936				Tail	Epididymomyoma		Per Wyatt and Khoo
Baillie	1936				Tail	Epididymomyoma		Per Wyatt and Khoo
Baillie	1936				Tail	Epididymomyoma		Per Wyatt and Khoo
Charache	1939	43WM	10 yrs.	3	Left, tail	Lymphangioma	Excision	7 yrs.; doing well
Falconer	1939	72				Adenofibromyoma		At autopsy
Nakamura	1939	37	17 yrs.	2x0.5x1.5	Right	Lymphangioma simplex		
Halpert	1941	60CM		3x2x1.5		Mixed leioma-lymphangioma	Epididymectomy	On epididymis
Blumer and Edwards	1941	54WM	40 yrs.	3x4		Adenoma	Excision and hydroceleotomy	"In testis"
Gordon-Taylor, Ommaney-Davis	1941		"wks"		Left	Adenoma	Orchiectomy	
Masson et al	1942	31	18 mos.	2x1.5	Left, tail	Mesothelioma		
Masson et al	1942	29		Pea	Left, tail	Mesothelioma		Pain 4-5 days
Masson et al	1942		2 yrs.	Nut	Right	Mesothelioma		
Evans	1943	53WM	3 yrs.	1.5	Tail	Mesothelioma	Excision	1 yr.; doing well
Evans	1943	36	3 mos.	2		Mesothelioma	Excision and orchiectomy	11 mos.; doing well
Evans	1943	30	"yrs."	2	Mixed	Mesothelioma	Excision	"No recurrence"
Evans	1943	55	4 yrs.	1		Mesothelioma	Resection	"Patient well"
Malisoff and Helpern	1943	57WM	3 days	2	Right, head	Leiomyoma-lymphangioma	Orchiectomy	
Golden and Ash	1944	29WM		1.5	Right, tail	Adenomatoid	Excision	
Golden and Ash	1944	23WM	6 mos.	2	Head	Adenomatoid	Excision	
Golden and Ash	1944	28WM		2.5	Right	Adenomatoid	Excision	
Golden and Ash	1944	32WM		1.5		Adenomatoid	Epididymectomy	
Golden and Ash	1944	26WM	3 yrs.		Head	Adenomatoid	Orchiectomy	
Golden and Ash	1944	44WM	5 yrs.	1	Left, tail	Adenomatoid	Epididymectomy	4½ yrs.; alive, well
Golden and Ash	1944	21WM		1	Right	Adenomatoid	Excision	
Golden and Ash	1944	26WM	8 mos.	1.5	Left, tail	Adenomatoid	Excision	
Golden and Ash	1944	33WM		Bean	Right	Adenomatoid	Excision	
Golden and Ash	1944	34	3 yrs.		Tail	Adenomatoid	Resection	
Golden and Ash	1944	68CM			Left, tail	Adenomatoid		Incidental at autopsy
Golden and Ash	1944	22CM	2 wks.	0.5	Left, head	Adenomatoid	Excision	
Golden and Ash	1944	38WM	5 yrs.	1	Tail	Adenomatoid	Epididymectomy	
Baird	1944							According to Lee et al
Robinson	1945	30WM	5 yrs.	2.5	Left, tail	Mesothelioma	Epididymectomy	
Robinson	1945	28WM	4 yrs.	2.5	Left, tail	Mesothelioma	Epididymectomy	
Sworn, Marshall and Edwards	1946	34	"yrs."		Right, tail	Adenomatous	Excision	
Sworn, Marshall and Edwards	1946	43	2 yrs.		Left, tail	Adenomatous	Excision	

TABLE 2 (Continued)

Author	Year	Case	History	Size (Cm.)	Location	Diagnosis	Treatment	Miscellaneous
Bo[illegible]e, Cristol and Devers	1946	42	13 yrs.	4	Left, tail	Benign solid tumor	Orchiectomy	1 yr., negative
Morehead	1946	62WM		1x1.5	Tail	Angiomatoid	Epididymectomy	
Foot	1946					Angiosarcoma		
Foot	1946					Angiosarcoma		
Foot	1946					Angiosarcoma		
Codnere and Flynn	1946	26	10 mos.	2	Left, head	Adenomatoid	Epididymectomy	
Codnere and Flynn	1946	33	7 yrs.	2.5	Right, head	Adenomatoid	Epididymectomy	1 yr.; doing well
Codnere and Flynn	1946	47		1	Right, head	Adenomatoid	Excision	
Beneventi	1947	38	4 mos.	2x1.5	Left, tail	Lymphangioma	Excision	
Falconer	1947	39	5 mos.	Nut	Right	Adenofibromyoma	Excision	
Falconer	1947	36	6 yrs.	Nut	Right	Adenofibromyoma	Epididymectomy	
Patterson and Mogg	1947		1 yr.	2.5	Right, head	Mesothelioma	Excision?	
Fajers	1948	27	6 yrs.	Pea	Right, tail	Lymphangioma	Excision	39 yrs.; doing well
Fajers	1948	35	3 mos.	1x1.5	Left, tail	Angioma	Excision	12 yrs.; doing well
[illegible]iers	1948	50	1 yr.	1	Left, tail	Angioma	Excision	10 yrs.; doing well
[illegible]ajers	1948	45	5 yrs.	Bean	Right, tail	Angioma	Excision	3 yrs.; doing well
[illegible]ajers	1948	58	2 yrs.	Walnut	Right, tail	Lymphangioma	Excision	2 yrs.; doing well
[illegible]ilson	1949	46	3 mos.	1.5	Left, tail	Adenomatoid-leiomyoma	Excision	
Burros and Mayock	1950	5 mos. WM		3		Adenomatoid	Radical orchiectomy	
Wyatt and Khoo	1950	56WM		3.5	Right, tail	Adenomatoid	Orchiectomy	
Wyatt and Khoo	1950	45WM		1	Tail	Adenomatoid		At autopsy
Glaser	1950	37	10 days		Right, tail	Lymphangioma	Excision	
Glaser	1950	57	4 mos.		Left	Hemangioma	Epididymectomy	
Longo et al	1951	42	4 yrs.	3x2	Left, tail	Adenomatoid	Epididymectomy	Lived 26 yrs.
Longo et al	1951	31	6 yrs.	2x1.5	Left, tail	Adenomatoid	Excision	26 yrs.; doing well
Longo et al	1951	49		2x1.5	Left	Adenomatoid	Excision	Lived 3 yrs.
Longo et al	1951	44	5 yrs.	1.5	Right, tail	Adenomatoid	Epididymectomy	17 yrs.; doing well
Longo et al	1951	46	1½ yrs.	1	Right, tail	Adenomatoid	Excision	11 yrs.; doing well
Longo et al	1951	49	16 yrs.	2.5	Right, tail	Adenomatoid	Excision	8 yrs.; doing well
Longo et al	1951	50	7 yrs.	3	Right, tail	Adenomatoid	Epididymectomy	1 yr.; doing well
Longo et al	1951	42	2 yrs.	2	Left, head	Adenomatoid	Excision	4 yrs.; doing well
Longo et al	1951	34		2x1.5	Left, head	Adenomatoid	Orchiectomy	4 yrs.; doing well
Longo et al	1951	58		1.5	Left	Adenomatoid	Excision	4 yrs.; doing well
Longo et al	1951	60		3x3	Right, tail	Adenomatoid	Orchiectomy	2 yrs.; doing well
Longo et al	1951	61	1½ yrs.	3x3.5	Left	Adenomatoid	Orchiectomy	1 yr.; doing well
Falk and Konwaler	1951	38CM		1x1x1.5	Head	Adenomatoid	Radical orchiectomy	3 mos.; doing well
Meeter and Schwartz	1951	32	3 yrs.	5	Right, tail	Adenomatoid	Epididymectomy	4 yrs.; doing well
Meeter and Schwartz	1951	60	5 yrs.	2	Right	Adenomatoid	Epididymectomy	1 yr.; doing well
Mylius	1952	43	10 yrs.	Nut	Left, tail	Mesothelioma		
Mylius	1952	52	3 mos.	Pea	Tail	Mesothelioma		
Mylius	1952	52	2 yrs.		Left	Mesothelioma		
Mylius	1952	40	6 mos.	Nut	Right, tail	Mesothelioma		
Mylius	1952	36	2 mos.	Nut	Left	Mesothelioma		
Duffy	1953	54	6 yrs.	1.5	Left, tail	Adenomatoid	Excision	Slow growth
Rapoport and Morgan	1953	26WM	5 yrs.	2x2.5	Tail	Adenomatoid	Excision	Painless
Rapoport and Morgan	1953	54	31 yrs.	2	Head	Adenomatoid	Excision	Painless
Sundarasivarao	1953	41		0.8	Left, head	Adenomatous		At autopsy
Sundarasivarao	1953	51		1.2		Adenomatous	Excision	
Sundarasivarao	1953			2.5	Tail	Adenomatous		
Sundarasivarao	1953	54	25 yrs.	1.2	Right	Adenomatous		
Sundarasivarao	1953		2 yrs.	2		Adenomatous		
Sundarasivarao	1953	20	17 mos.			Adenomatous		Hormone disturbance
Cameron	1954	66WM		1.5		Adenoma	Excision and herniorrhaphy	Incidental
Wentzell	1954	57WM	"wks"	1.5	Right, head	Adenomatoid	Excision	
Wentzell	1954	29WM	6 mos.	1.5	Left, head	Adenomatoid	Excision	Painful
Lazarus and Friedman	1954	70WM	1 yr.	3.5	Right, tail	Fibroleiomyoma-lymphangiosarcoma	Orchiectomy	2 mos.; doing well
Teilum	1954	63		1.5		Mesothelioma	Excision	
Gibson	1954	55	3 yrs.	Cherry	Right, tail	Adenomatoid	Excision	Tender
Sorensen	1955	53WM	15 yrs.	20 Kg.	Left	Angioleiomyoma (adenomatoid)	Enucleation and repair	Huge tumor
Gueukdjian	195[illegible]							Data incomplete
Curtiss and Hock	19[illegible]	34WM			Tail	Adenomatoid	Orchiectomy	
Morin	19[illegible]	48WM	15 yrs.	2x3	Left, tail	Adenomatoid	Epididymectomy	Bilateral tumors
Morin			3 yrs.	1	Right, tail	Adenomatoid	Excision	

TABLE 2 (Continued)

Author	Year	Case	History	Size (Cm.)	Location	Diagnosis	Treatment	Miscellaneous
Rankin	1956	40	"wks"	1.8	Right, tail	Adenomatoid	Excision	
Jablokow	1956	51WM	1 yr.	1.5	Right, tail	Adenomatoid	Excision	
Glenn	1956	64CM	13 yrs.	3x3x4	Left, tail	Adenomatoid	Orchiectomy	3 mos.; doing well
Glenn	1956	37WM	15 yrs.	2	Left, tail	Adenomatoid	Orchiectomy	No recurrence
Glenn	1956	71WM	50 yrs.	1	Left, tail	Adenomatoid	Orchiectomy	No recurrence

plasms than the epididymis.[40] About 75% of all primary epididymal neoplasms are benign, and approximately two-thirds of these are adenomatoid tumors. Thus roughly 50% of all primary tumors of the epididymis are adenomatoid tumors. A classification of epididymal tumors is presented in table 1. Adenomatoid tumors also occur in the tunica vaginalis[8,41] and spermatic cord,[42,43] and are also found in the female genital tract, predominantly along the posterior aspect of the uterus and tubes.[19,44,45]

During the past 10 years there have been about 4,300 autopsies, over 100,000 surgical specimens, and more than 300,000 new patients seen at these institutions. (The Duke Hospital and the V. A. Hospital, Durham.) In searching the records, only 3 authentic cases of adenomatoid tumor of the epididymis were found, although a number of fibromas and lipomas of the epididymis, tunics and cords were noted. In addition, one adrenal rest tumor of the epididymis and one fibrosarcoma of the epididymis with metastases have been seen here. It is estimated that the incidence of adenomatoid tumors is slightly less than one-half of all primary epididymal tumors seen here.

A total of 120 authentic cases of adenomatoid tumor of the epididymis are recorded in the literature.[1-4,6,7,9,10,12-14,16-19,29-40,44,46-77] To these may be added the 3 patients reported here. The total 123 recorded instances of adenomatoid tumor of the epididymis are abstracted and summarized in table 2. No cases are included in which any doubt exists as to diagnosis, and no tumors arising elsewhere than in the epididymis are included.[8,41,42] Other reports in the literature[78-92] suggest that possibly a number of epididymal tumors variously recorded as angioma, myosarcoma, leiomyoma, and myomatous tumors might actually be adenomatoid tumors, but since the data is incomplete, these cases are not included.

Clinical features. The major clinical features of adenomatoid tumors may be summarized from the tabulated cases. The most common presenting symptom was of a painless mass in the region of the testis, though often the tumor was discovered incidentally during routine examination. Pain was a prominent feature in only about 20% of the reported cases, and a significant hydrocele was present in only 15%, though a small amount of fluid in the tunica was the rule. Predisposing factors of trauma, venereal disease, epididymitis, infection of the urinary tract, or hormonal imbalance cannot be implicated consistently.[11,20]

Adenomatoid tumors are generally small, averaging less than one inch in diameter. The average age of patients is 42 years, but instances have been reported in the newborn[63] and in a man of 78 years.[1] Where race has been mentioned, the tumor predominates in Caucasians, only 4 instances of adenomatoid tumor of the epididymis having been noted specifically in Negroes. Duration of the mass prior to operation averages about 2 years, though many cases were found as incidental autopsy findings, and there is one instance of nearly 50 years duration in this study (Case 3). A slightly greater predilection of the tumor for the left epididymis than the right has been noted. Adenomatoid tumors of the epididymis are found four times as frequently in the tail as in the head and body of the organ according to this survey.

Recurrence. The histogenesis of adenomatoid tumors of the epididymis remains obscure, but it is apparent from a review of the literature that these tumors exhibit no malignant characteristics.[93] Despite various modes of therapy employed, no instance of recurrence or metastasis of an adenomatoid tumor of the epididymis has been recorded. This is in sharp contrast to mesotheliomas which do metastasize, raising another point of difference between these two categories of neo-

plasms. It is notable that follow-up of patients has extended to 26 years after treatment without evidence of recurrence of metastasis.

Therapy. The clinical course and pathologic nature of adenomatoid tumors of the epididymis thus indicate that any treatment more than excision of the lesion is unnecessary. It is of utmost importance that suspected adenomatoid tumors of the epididymis be differentiated from other intrascrotal masses, such as testicular tumors, spermatocele, epididymitis, torsion, orchitis, and hydrocele. If accurate clinical appraisal can be made, the surgical approach may be modified, since simple excision or resection of adenomatoid tumors is all that is indicated. Such conservative treatment carries with it the psychologic and functional advantages of preserving normal genital structures.

Summary

1. Three additional cases of adenomatoid tumor of the epididymis are added to 120 cases already in the literature, and the clinical and pathologic features of all 123 cases are studied.

2. No completely acceptable theory of origin of adenomatoid tumors has been found, though evidence points to mesothelial origin.

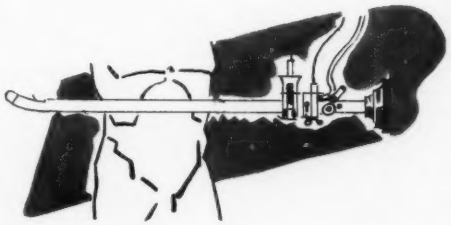
3. Histochemical studies of adenomatoid tumors of the epididymis indicate unusual metabolic characteristics which prompt fresh speculation as to origin of these tumors.

4. Conservative surgical therapy of adenomatoid tumors of the epididymis is urged in view of the benign nature of the lesions.

Acknowledgment

The author wishes to thank Dr. Albert G. Smith, Department of Pathology, and Dr. E. P. Alyea, Chief of Urology, for their assistance and encouragement in this study.

The list of references will appear with the author's reprints.



Strangulated Hemorrhoids:

Deep Radiotherapy or Surgical Treatment*

ENRIQUE FIGARES, M.D.,† *Havana, Cuba*

The author considers the results with either type of treatment.

THE THROMBOSIS of prolapsed and irreducible internal hemorrhoids is generally known as strangulated hemorrhoids. The so-called strangulation is due to thrombophlebitis rather than to any strangling effect from spastic sphincter which is generally hypotonic. The investigating finger may easily be introduced into the anal canal revealing the absence of true strangulation. Such thrombophlebitis is the most serious and painful of all complications caused by hemorrhoids.

In appearance strangulated hemorrhoids is like that of an inflamed growth outside the anus, formed by double circular folds in which may be seen, all the constituents of "phlegmasia alba dolens;"—edema, thrombus and cellular infiltration. In some instances only half of the anus is affected. At the periphery the skin takes on this inflammation forming a white or pinkish-white fold, and small thrombi may be encountered when transparency permits. The interior round fold of the edema is of dark red or purplish color and is formed by internal thrombotic and inflamed prolapsed hemorrhoids (Fig. 1, A). Between these two folds there is a deep line, corresponding to the pecten band. By making a radial incision in these two circular folds, numerous clots of varied size and at different levels may be observed inside; some of these are invisible through the transparent areas (Fig. 1, B). This condition may appear suddenly in patients in whom the least effort causes protruding internal or mixed hemorrhoids.

Spontaneous evolution occurs after three or four weeks of intense pain, the patient being bedridden meanwhile.

Opinions are greatly divided as to the system to be employed in the treatment of this painful complication. Some favor immediate surgical intervention, while others advise palliative measures, postponing surgical treatment.

Radiotherapy

For several years we have been employing anti-inflammatory radiotherapy, so highly recommended by Bensaude[1] in 1934, with magnificent results and no complications.

This is not a destructive technic, the rays employed are weak and do not penetrate deeply. In treating men, the testicles are protected by inclining the radiation cone, and in case of necessity, by lead plaques. In women, the weak rays used and the deep location of the ovaries have never given rise to any genital accidents.

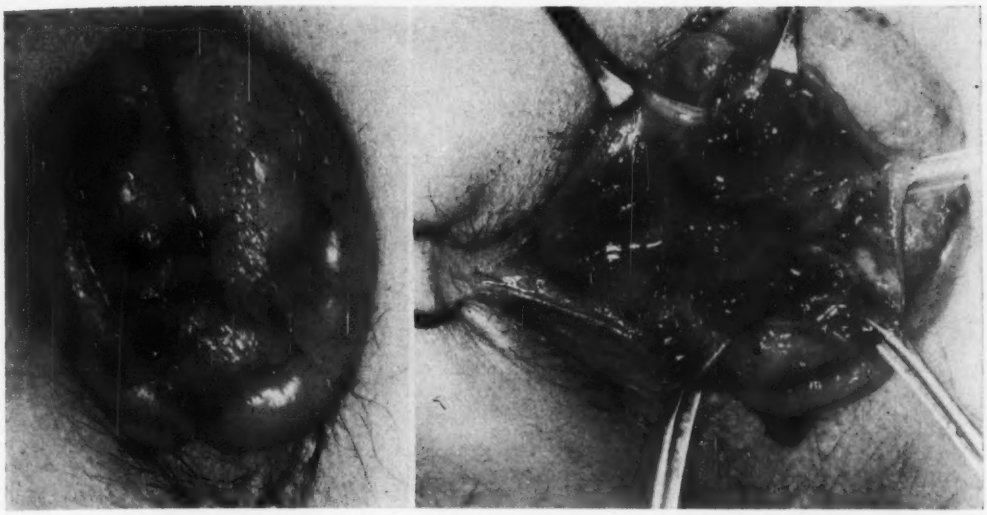
Technic. We employ 150 r. at intervals of one to three days for two or three sessions. The factors are as follow: 200,000 V., 15 ma., at 50 cm. distance, copper and aluminum filter of 1 mm. At the first session 150 r. are given to a perineal field, the patient being in a prone position. The buttocks are separated by the assistant or the patient himself, so that irradiation is directly over the area of the thrombosed hemorrhoids.

After the first passing exacerbation which all radiotherapy produces, the pain recedes and edema is reduced. After the second application, a day or two later, and with a dose of 150 r., recovery is noticeable. A half hour after the second treatment the patient feels that the inflammation is reduced, and is often heard to remark, "I feel a drawing sensation inside the inflamed parts." This odd sensation lasts for about sixty minutes. Following the third application, the patient again feels this same drawing sensation inside the hemorrhoidal growth, but to a lesser degree than after the second application.

*Read before the Section on Proctology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

†From the Proctological Section, Department of Surgery, Mercedes Hospital, Vedado, Havana, Cuba.

FIG. 1



A B

(A) Strangulated hemorrhoids. (B) A radial incision shows thrombi of various sizes and at different levels.

Comment

We have treated many cases with excellent results. In the majority pain decreases after the second irradiation, and in some instances recovery is noticeable, even after the first session. In other cases pain stops quickly, but the size of the growth does not diminish, though it does not seem to bother the patient who is able to be up and about and even may go back to work without apparent inconvenience. Rapid results are best obtained when the radiotherapy treatment is applied as soon as possible (Figs. 2 and 3). With this treatment we have been able to give rapid relief to many patients suffering from this most painful hemorrhoidal complication.

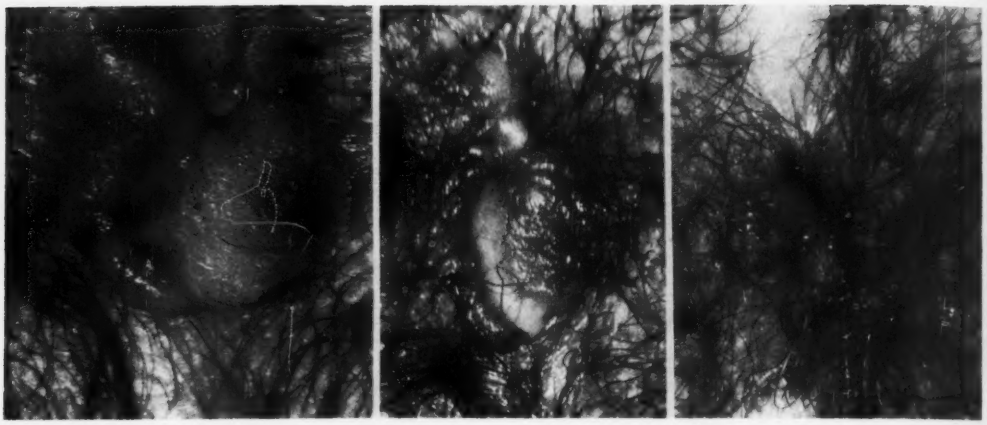
This technic reduces the hemorrhoidal crisis, but does not cure the hemorrhoids. The patient, who has undergone such a treatment and apparently seems to be cured, continues to suffer from hemorrhoids and is susceptible to further crises in the future.

FIG. 2

A B C

(A) Before treatment. (B) 7 days after treatment. (C) 10 days after treatment.

FIG. 3



A B C

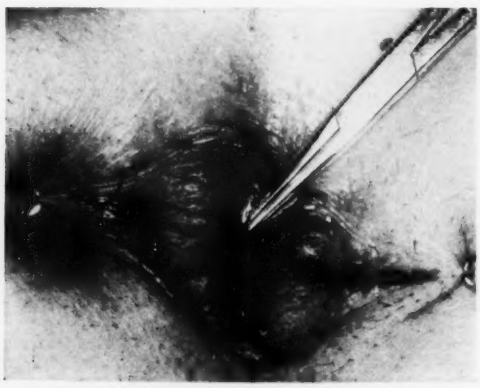
(A) Before treatment. (B) 8 days after treatment. (C) 15 days after treatment.

Surgical Treatment

If the patient is seen two or more days after the beginning of the trouble, surgical treatment is advised for the following reasons: (1) If medical treatment is employed the patient will be bedridden for over a week, suffering pain; (2) if operation is performed, the time period is the same, but there is less pain and a final cure.

Facing a hemorrhoidal complication, the surgeon often finds himself in a quandary as to which surgical technic to use in the extirpation of all thrombi and hemorrhoidal varicose veins, and the restoration of the anal canal to its normal condition and appearance.

FIG. 4



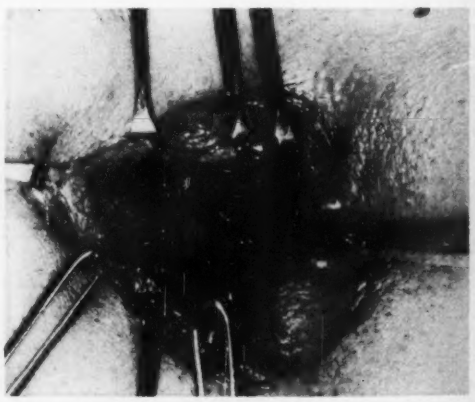
The radial incision is marked with ink.

The technic described by Rakov,[2] in 1945, under the title of "Hemorrhoidectomy by Incision and Dissection," is the most satisfactory and easily carried out, and gives the best results in this most serious hemorrhoidal complication. We[3] employ hypobaric spinal anesthesia with Nupercaine 1:1500, 3.5 cc., plus 0.2 cc. of Neo-Synephrine, 1%, producing anesthesia lasting from 8 to 12 hours.

Technic. This consists of an incision and the dissection of the hemorrhoidal mass:

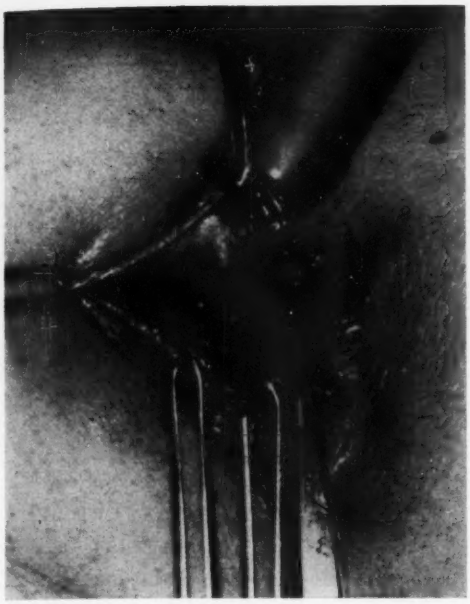
1. An Allis forceps is adjusted in the skin, next to the edema caused by thrombophlebitis; another forceps, in the healthy mucosa next to the thrombi (Fig. 4).

FIG. 5



The radial incision reaches as far as the subcutaneous portion of the external sphincter. The lips being held by Allis forceps.

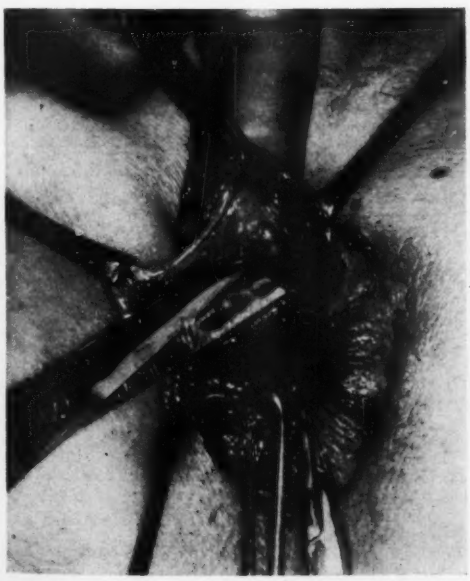
FIG. 6



An Allis forceps is employed and the index finger used to evert the internal surface.

2. A radial incision is made across the center of the hemorrhoidal mass, from one forceps to the other, and to a depth reaching the subcutaneous fibers of the external sphincter (Fig. 5).

FIG. 7



Curved scissors are used for the dissection of the thrombi.

FIG. 8

Both flaps are dissected.

3. The lips of the incision are held by Allis forceps (Fig. 5).

4. Treating each half of the incision separately, handling the Allis forceps, the thumb facing front and the three last fingers held underneath; the index finger, which remains free, is placed on the external surface of the flap of the wound, thus making the internal area somewhat more prominent by means of slight pressure applied in the area of the thrombi, that is to say, the flap is turned outward or everted, thereby exposing the deeper area (Fig. 6).

5. With curved scissors, using the convex side, the thrombi and hemorrhoidal tissues are dissected. The assistant aids by grasping a clump of hemorrhoidal tissue with toothless thumb forceps (Fig. 7).

6. The other flap of the incision is dissected in the same way (Fig. 8).

FIG. 9

A Buie clamp holds the lips of the flaps to be cut away.

7. Little arterial bleeding results and is stopped with fine catgut. The venous hemorrhage ceases spontaneously.

8. Having cleaned both flaps of the wound, the excess tissue of the surrounding area is cut away. To do so, the incision is stretched and held at both ends with two straight forceps and the lips of the wound are then drawn together with Allis forceps.

9. A curved Ochsner forceps or a Buie clamp is held under the Allis forceps, the full length of the incision and well adjusted to it. With the scalpel the excess tissue is cut away (Fig. 9).

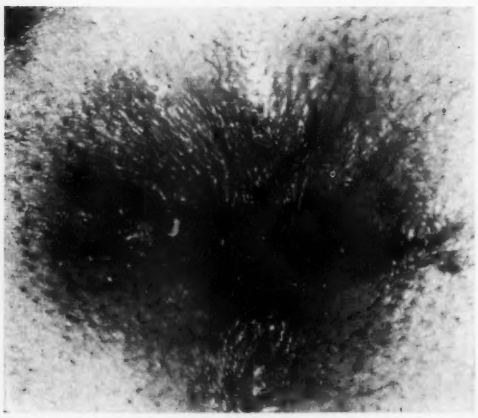
10. Similar incisions are made in the other hemorrhoidal masses. Often an incision made at the center of each side of the anus, is sufficient for the dissection of the thrombi, when situated at the inner or outer edges (Figs. 10 and 11).

Comments

In cases of complicated hemorrhoids this surgical technic is quite easy to carry out, bleeding is reduced to a minimum and dissection is rapidly effected.

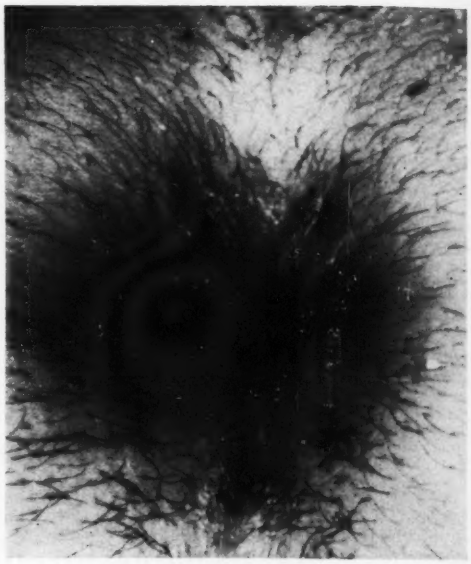
The postoperative period following this technic is not painful, easily endured, and in a majority of cases the administration of a sedative has been found unnecessary. Furthermore, the long-lasting hypobaric spinal anesthesia is of great help in the well-being of the patient during the first few hours. Among the many cases operated on by us, we have had only one presenting pulmonary embolism, which was favorably overcome; but we are well aware that such a complication may also arise in patients treated medically and cannot affirm that the surgical treatment tends to produce pulmonary thrombosis.

FIG. 10



End of operation.

FIG. 11



Same case 13 days following operation.

Summary

1. Strangulated hemorrhoids is the most serious and painful of all complications caused by hemorrhoids.

2. The anti-inflammatory radiotherapy treatment is giving magnificent results with no complications.

3. The dose employed consists of 150 r. at intervals of one to three days for a total of two or three sessions.

4. Rapid results are best obtained when the radiotherapy treatment has been applied within 48 hours. After this period, surgical measures are advised.

5. Surgical treatment consists of the incision and dissection of the hemorrhoidal mass.

6. The postoperative period is not painful, healing is rapid and final results satisfactory.

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Discussion (Abstract)

Dr. Claude G. Mentzer, Miami, Fla. I am glad to have the privilege of discussing Dr. Figares' paper. If his paper were presented in debate form: *Resolved, that so-called strangulated hemorrhoids should be treated with x-ray therapy preliminary to surgery,* I would have to take the negative side because, first, I have had no experience with this technic, and second, my approach to the treatment of this condition has been highly satisfactory.

Prior to the use of antibiotic therapy, deep radiation technic was used in treating a critical condition, cavernous sinus thrombosis. In thrombosed hemorrhoids, however, we are not dealing with a critical condition, and I feel there are other approaches which are preferable.

If you believe in palliation therapy directed toward lessening the acute condition of pain, edema and thrombosis, then an antihistamine combination, devised by Marks and used by him and others, has proven of great value. This treatment is cheaper, simpler, and offers less hazard to the patient than radiation therapy.

It is my opinion and has been my experience, however, that immediate definitive surgery offers the most to these patients. Twenty years ago, Dr. Cartwright sent a questionnaire to all members of the American Proctologic Society relative to their treatment of thrombosed hemorrhoids. For every one doctor who advised a waiting, quieting down period before doing definitive surgery, two doctors advised immediate surgery. In adhering to this approach, that is, immediate, definitive surgery, in my experience there has been no more postoperative pain than when an ordinary hemorrhoidectomy is done. The healing time is approximately the same, the functional and cosmetic results are excellent, and there have been no complications, such as postoperative stenosis, embolic phenomena or hemorrhage.

For the foregoing reasons, I feel that radiation therapy is unnecessary in most cases. The delay in doing definitive surgery adds to the patient's pain and lengthens his time away from work, thereby increasing the cost to him. I would reserve this radiation measure for the poor risk patient where other palliative measures have failed to give him relief.

Again, Dr. Figares, I wish to thank you for giving me the privilege of discussing your paper.

Fifty-third Annual Meeting of Southern Medical Association in Atlanta, Ga., November 16-19, 1959

Setting Up an Isotope Laboratory in an Average Hospital*

GEORGE J. CARROLL, M.D., and HERMAN MIZE,† *Suffolk, Va.*

The diagnostic and therapeutic use of radioactive isotopes is rapidly moving into a place of daily need in the practice of medicine. Thus, such use will not be limited only to the larger medical centers.

THE ESTABLISHMENT OF AN ISOTOPE LABORATORY in our hospital of 155 beds was contemplated for almost a year before it was believed that the program would be feasible. It has been stated that our bed capacity is borderline for the practical use of isotopes, and further that it is probably only of importance in the diagnosis and treatment of thyroid disease. We see a fair number of thyroid or potential thyroid patients in a year's time but we are not in a typical thyroid belt. Although we hoped to have a varied type of isotope program, it seemed that, I^{131} uptake studies would still be the sustaining activity in our laboratory. Any clinical pathologist in a hospital of the size of ours is usually acquainted with the vast majority of clinical problems. After analysis it appeared that our program would best fit our needs by adding other of the isotope technics which have become available. In this way we could not only do the routine studies, but also include clinical research problems which might arise as the program progressed. I therefore, obtained a license for I^{131}, RISA, Fe^{59}, Cr^{51}, Co^{60}, P^{32} and I^{131} Rose Bengal.

The first part of this paper is a short discussion relating to the establishment of our program, since, in talking with others, it seems to be of great interest particularly because of the size of our hospital. The second portion will be devoted to a discussion of a few of the clinical problems which we have encountered and which will indicate the value of our program during its beginning.

*Read before the Section on Pathology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

†From the Department of Pathology, Louise Obici Memorial Hospital, Suffolk, Va.

Discussion of Laboratory Facilities

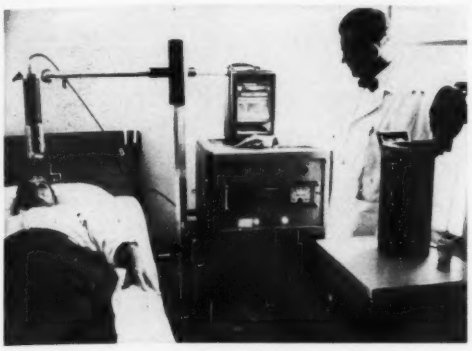
It is surprising how often the question has arisen as to the cost of such a program, the amount of necessary space, and what reaction and cooperation we have had from the medical staff, and finally, how successful our program has been. Our staff, through a direct approach at various meetings, had expressed a desire for some time for an isotope laboratory. This interest is, of course, only proportional to the interest of the person who wishes the program in his hospital. After realizing that the interest was there, I requested from the hospital administrator and board of directors the establishment of such a program and the necessary funds for equipment. This was approved and for the first year an appropriation of $4,000.00 was made. I obtained my license to use the most of the readily usable isotopes available for hospital use at the present time. I obtained this by commuting to Washington once a week for a period of 3 months.

The equipment necessary for the efficient operation of a unit in a hospital the size of ours must be compact and adaptable to perform procedures available. The following items are suggested; the approximate prices are given. These were selected upon advice as to practicability and economy, and are as follow:

Scaler with rate meter	$1,000
Scintillation probe and crystal	$ 385
Survey meter	$ 360
Lead bricks	$ 85
Lead pig	$ 50
Cart with arm	$ 325
	$2,205

This is the equipment essential for thyroid studies, but with a few more instruments at a

FIG. 1



Corner of BMR and tranfusion room where clinical isotope work is performed.

reasonable further cost, additional procedures which we wished could be done. These include blood volume, cardiac outputs, liver, pancreatic and kidney function studies, and hematologic procedures. For these an additional $1,500 is needed bringing the total cost to approximately $3,700. These instruments are:

Esterline Angus recorder	$ 360
Rate meter (ours is built into scaler)	$ 300
Well counter	$ 850
	$1,510

The purchase of this equipment must be made with care to be sure that all will operate with the basic scaler and in addition can be used in series. Glassware, of course, is a necessity but ours was obtained from the clinical laboratory. It is a good idea to utilize the film badge service. This can be processed in the hospital, but the added expense is small, especially since an outside agency provides a permanent record of exposure. Diagnostic and therapeutic isotopes have been made available for many sources. All the companies calibrate their products and all the prices are about the same. The biggest factor to the hospital is delivery service. In our laboratory we have found it more practical to purchase in bulk and measure our own dosage rather than to use radiocaps. We find it less expensive, especially with a daily variable number of patients. It allows us to schedule patients for study when we desire, daily if necessary.

For the clinical, as well as for average clinical research purposes a laboratory does not have to be large. We utilize portions of two rooms both of which can also be used for other purposes. Our clinical room is one also used for basal metabolic rate determinations, transfusions and other clinical work where a bed is needed (Fig. 1). We prefer our patients in a recumbent position, although for thyroid studies, the chair suffices. Our filing and secretarial work is done in the regular secretary's office of the laboratory where the files and records are kept. Our "hot room" is in the morgue, an out of the way spot for the receiving, handling, storage and preparation of the radioisotopes (Fig. 2). In it we have a room equipped with water and sinks, and a room with a low counting range. A table was built by our maintenance department with a stainless steel top and here is kept all our radioactive material. An icebox is available in the morgue for materials which must be kept cool. Shielding is accomplished by lead pigs and lead bricks. Pipetting can be easily accomplished at the height of the special table.

Illustrative Cases

In discussing our clinical material we are not drawing statistics, but merely wish to show how useful the program has been in aiding the laboratory and clinician in daily work. In our community I am fairly close to both the surgical and medical men and thus am aware of the major clinical problems in the hospital. This is one of the reasons why I believe a program such as ours can be of definite value in a smaller hospital.

Case 1. A 29 year old white woman was admitted to the hospital with a 2 week history of nervousness and weakness.

FIG. 2

"Hot room" in a portion of morgue. Table, lead bricks, lead pigs, automatic pipetter.

T. was 99°, P. 104, R. 20, and B.P. 120/78. Physical examination revealed no gross findings, and laboratory data was within normal limits. The x-ray findings were essentially normal. The EKG showed sinus tachycardia with some depression of the ST segment and flattening of the T waves.

On the day of discharge from the hospital, the patient was given 20 microcuries of I^{131}. She returned the following day, as an outpatient, for the 24 hour determination. The I^{131} uptake was 60 per cent. We decided to re-check this patient further; 2½ weeks later another study was done. At this time 50 microcuries were administered to do a protein-bound iodine conversion ratio as well as thyroid clearance curve (Fig. 3). The 24 hour uptake was 64 per cent. The uptake per hour was 11.25 per cent. The thyroid clearance ratio was 142 ml. per min. (This is definitely elevated over the upper normal limits of 38 ml. per min.). The P.B.I. conversion ratio was 79 per cent, which is in the hyperthyroid range.

Comment. We used the following formula to arrive at the thyroid clearance:[1]

Thyroid clearance rate: $\frac{\text{Average time interval uptake}}{\text{Total time equivalent to above}}$

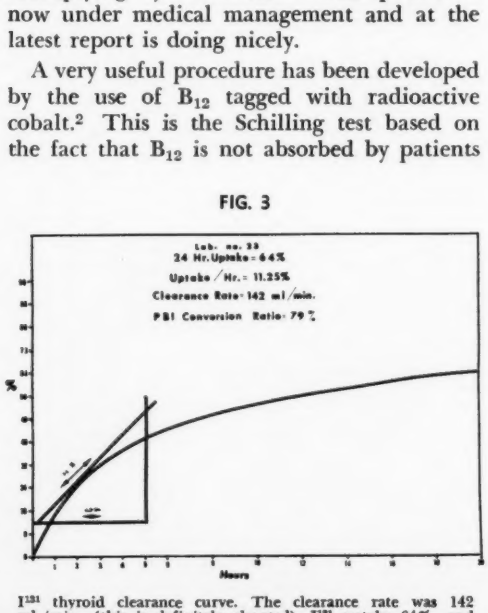
% L plasma conc: $\frac{\text{C/m Pl x 100 x 1000}}{\text{C/m St x dil x dose}}$

Thyroid clearance rate: $\frac{\text{Uptake/hour}}{\text{Plasma conc: x 60}}$

The thyroid clearance so determined equals the percentage per liter per minute clearance of the plasma by the thyroid gland of I^{131}. This can be converted to ml. per minute by multiplying by a thousand. This patient is now under medical management and at the latest report is doing nicely.

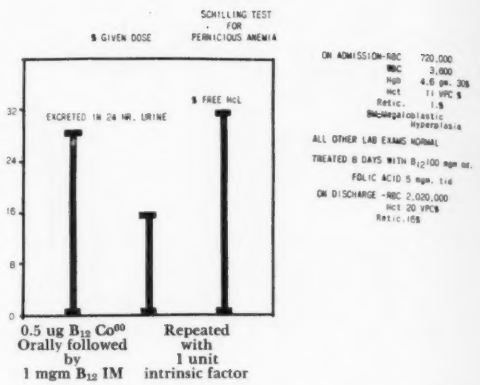
A very useful procedure has been developed by the use of B_{12} tagged with radioactive cobalt.[2] This is the Schilling test based on the fact that B_{12} is not absorbed by patients

FIG. 3



I^{131} thyroid clearance curve. The clearance rate was 142 ml./min. (this is definitely elevated), I^{131} uptake 64%, and P.B.I. conversion ratio 79 per cent.

FIG. 4



with pernicious anemia in the absence of the intrinsic factor. When 0.5 mc. of Co^{60} vitamin B_{12} is given intramuscularly followed by a flushing dose of 1,000 mcg. in 2 hours of B_{12}, normal individuals will excrete 5 to 25 per cent of the radioactive material in a 24 hour collected urine sample. Patients with pernicious anemia will excrete less than this amount. If the test is repeated with intrinsic factor added, the urinary excretion of radioactivity by the patient with pernicious anemia rises to a normal range. This is demonstrated in the following case.

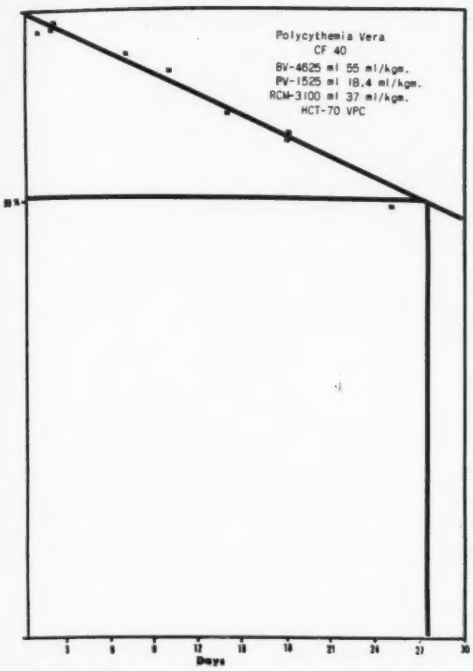
Case 2. A 44 year old white man was seen by us because of fatigue for one year.

On admission to the hospital his RBC was 720,000 per cu. mm., the Hgb. 5.6 Gm. and PCV 11 per cent. Examination of the peripheral smear revealed a macrocytic type of anemia. No free hydrochloric acid was present on gastric analysis before an injection of histamin but acid appeared following injection. The bone marrow study revealed a typical megaloblastic picture.

The patient was placed on B_{12} therapy and unknown to me, folic acid was added on the fifth day. His course was followed on an outpatient basis, and he returned after approximately 6 weeks when his RBC had risen to 4.5 million per cu. mm. At this time we did the Schilling test (Fig. 4). (The patient need not be in remission to perform the test.) Following administration of the B_{12} with Co^{60} 29 per cent radioactivity appeared in a 24 hour urine specimen. The test was repeated to check our own results with intrinsic factor added and the results were still within normal range.

Comment. This is not a true case of pernicious anemia because of free hydrochloric acid, but represents one of the other types of macrocytic anemias in which a megaloblastic type of bone marrow is found. Undoubtedly some of the cases previously diagnosed as pernicious anemia will ultimately be placed

FIG. 5



Red cell survival time was 27+ days. (Normal 25-35 days.) (Ordinate indicates percentage radioactivity remaining, abscissa length of time in days.)

with those of gastrointestinal malabsorption, liver disease or, as in this case, folic acid deficiency etiologically.

Case 3. A 36 year old negress was admitted to the hospital with chief complaint of attacks of weakness. She gave a history of having had hypertension for some years with headaches dating back some two or three years.

On admission the B.P. was 175/115. Examination revealed the eyelids to be puffy. The cheeks and lips had a definite reddish hue. The lungs were clear.

Laboratory data on admission revealed a RBC varying from 7,800,000 to 8,200,000 per cu. mm.; the Hgb. averaged 21.6 Gm. (143 per cent), the V.P.C. was 71 per cent. The N.P.N. was 51 mg. of 100 cc. Urine revealed a 3+ albumin. The total serum protein was 5.5 Gm., with an albumin of 3.68 and globulin of 1.87 Gm. The bone marrow revealed hyperplastic changes.

Medical consultation was had, and the diagnosis of idiopathic polycythemia was made.

A blood volume and red cell survival time were done using Cr^{51} (Fig. 5). The total blood volume was found to be 4,625 ml., plasma volume 1,525 ml., and red cell mass 3,100 ml. The red cell half life was 27 days, and with the dosage used was considered to be within normal limits.

The patient was discharged from the hospital and her course followed for a period of 3 weeks to complete the red cell survival studies. During this time her red cell count has ranged from 7,500,000 to 8,000,000 per cu. mm.

The patient was then treated with 3 mc. of P^{32} and is to be followed in our outpatient department.

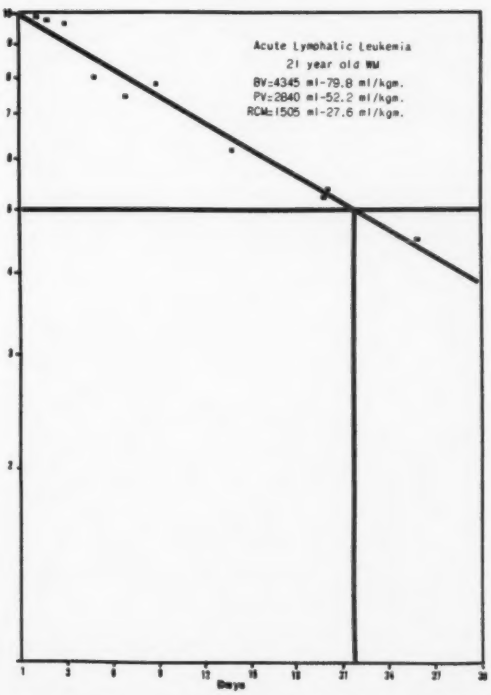
It is well accepted that patients with leukemia often develop a hemolytic syndrome terminally. We had such a patient whom I had the opportunity to observe and treat for a period of 9 months with Purinethol and Metacortin.

Case 4. On his final hospitalization for a period of 3 weeks, red cells in this 21 year old white man were tagged with chromium and a blood volume and red cell survival time were done (Fig. 6). The red cell mass was 1,505 ml., plasma volume 2,840 ml. and total blood volume was 4,345 ml. The red cell survival time revealed a half life of slightly over 21 days indicating an increased destruction of red cells.

Necropsy findings revealed a generalized process typical of lymphatic leukemia. A radiogram of the spleen, even after 3 weeks, showed a satisfactory response, indicating activity and pooling of blood.

We have been impressed by our blood vol-

FIG. 6



Total blood volume and red cell survival time using Cr^{51} on patient terminal with lymphatic leukemia. Red cell survival time is 21+ days. (Ordinate indicates percentage radioactivity remaining, abscissa length of time in days.) Patient shows evidence of hemolytic anemia.

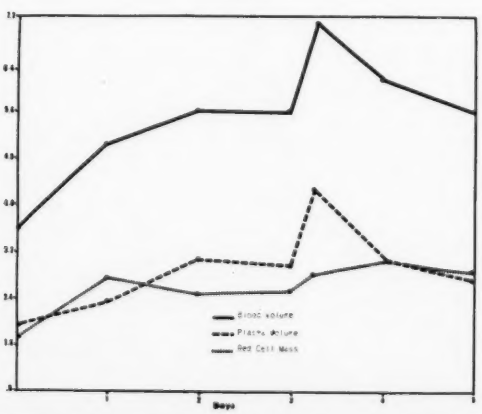
ume studies. In beginning our program we had no idea of the number of patients on whom we would be asked to perform blood volumes. I would like to present the findings on 2 patients to indicate the value which we and the surgeon believe can be attached to the values obtained. They are of indefinite value in the poor risk surgical patient, and the surgical patient who is seriously ill.

Case 5. A middle-aged white man was admitted to the hospital with beginning jaundice and evidence of gallbladder disease.

At exploratory laparotomy the head of the pancreas was found to show necrosis, proven by biopsy. The gallbladder was full of stones, but exploration of the common and hepatic ducts revealed no stones as a cause of the obstruction. The patient bled considerably during the operation, and was doing so poorly that a pint of blood, tagged with chromium, was administered during the surgical procedure.

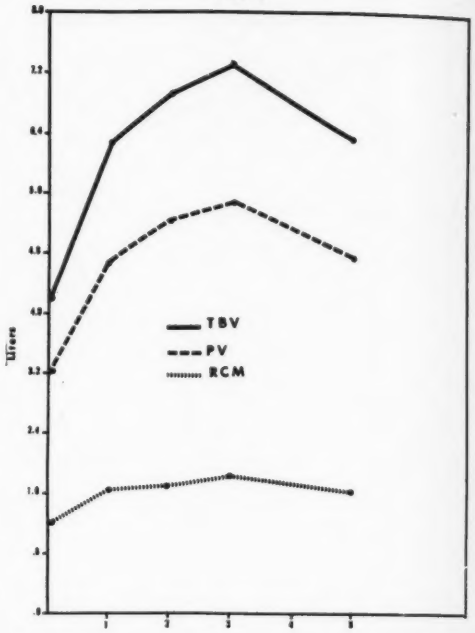
The first blood volume estimated was on the pint of tagged blood taken during the operative procedure (Fig. 7). During the first day, the patient received 3,900 cc. of fluid and of this 1,500 cc. was in whole blood. During this same period the patient excreted only 285 cc. of fluid. At the end of the first day the total blood volume has increased along with the red cell mass. During the second day, the patient received 3,000 cc. of fluid with no blood. During this time he excreted 1,140 cc. At the end of the second day, the total blood volume was again increased with the red cell mass, due to the dilution, decreasing in proportion to the plasma volume. During the third day, the rise in the blood volume coincided with receiving 500 cc. of whole blood. Between the third and fourth day, the patient received 2,470 cc. of fluid so that at the end of the fourth day his total blood volume was considerably elevated, and at this time the plasma volume and red cell mass were approximately 50 per cent. The

FIG. 7



Daily blood volume studies using Cr^{51} on patient with pancreatitis. (Abscissa length of time in days, ordinate-volume in liters.)

FIG. 8



Blood volume on a patient with gastrointestinal bleeding using Cr^{51}. Patient received total of five pints of blood from first to third days. (Ordinate indicates liters, abscissa length of time in days.)

following day, the patient received only 1,500 cc. of fluid and there began a decline in the values.

Comment. It was generally conceded that this patient was "overhydrated." Because of medical shock and inability at all times to determine any blood pressure level, an intravenous levophed drip was used to maintain the blood pressure in the vicinity of 100/50. The patient died in uremia; no autopsy was done.

Case 6. A 59 year old white man was admitted to the hospital with a history of vomiting of blood and bleeding hemorrhoids.

He gave a past history of over a period of a year. He had been studied at another hospital with negative findings. Two days before admission he passed a large tarry stool and vomited coffee-ground material.

The day following admission an upper gastrointestinal series showed hypertrophic gastritis with a shallow mucosal erosion of the gastric mucosa, thought to be the source of bleeding.

On admission the RBC was 3,150,000, WBC 18,800, Hgb. 9.7 Gm. (65 per cent).

A blood volume done on the day following admission revealed the following (Fig. 8). The TBV was 4,180 ml., P.V. 3,010 ml., RCM 1,170 ml. During the time of admission to the peak of the curve, the patient received 5 pints of blood, following which therapy was

stopped. His blood level tapered off and the patient was discharged on a medical regimen on the 8th hospital day. (He was discharged because he was uncooperative, and a more prolonged hospital stay which was advised was not accepted.)

Comment. The total blood volume determined by either a RISA or chromium method is a very acceptable means of performing total blood volume studies. There are some drawbacks to both methods. We prefer chromium over RISA mainly because the demand varies, and the one-half life of RISA is relatively short. This allows a far greater loss of RISA which can be expensive to the laboratory. Actually there are instances when RISA is to be preferred as the isotope of choice. Tagging with chromium, however, makes it only necessary to give one dose of the drug and the patient can be followed for a considerable period of time. Our method for the calibration of the blood volume is as follows:

Formula for Blood Volume

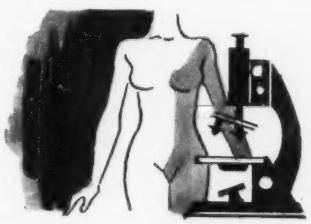
$$\text{RBV} = \frac{\text{cc/m whole blood standard}—[\text{cc/m plas. standard (1-c/hem)}]}{\text{cc/m pts. whole blood}—[\text{cc/m pts. plas. (1-c/hem)}]}$$

Conclusions

A radioisotope laboratory in a hospital the size of ours is useful. Its usefulness will depend to a large extent upon the interest of the pathologist. Since many of the useful diagnostic tests in use today parallel the work done in the clinical laboratory, the pathologist should become acquainted with, and involved in the management of such a laboratory in his hospital. This can be accomplished alone, through an isotope committee of which he is a member, or in collaboration with the radiologist.

References

1. Manual Radioisotope Laboratory U.S.N.H. Bethesda, Maryland, page 68.
2. Fields, T., and Seed, L.: Clinical Use of Radioisotopes, Chicago, The Year Book Publishers, Inc., 1957, p. 62.



Fractures of the Femoral Condyles:

Experiences with a New Design Femoral Condyle Blade Plate*

ROBERT B. ELLIOTT, M.D., *Houston, Tex.*

The author describes his experiences with a new device for the fixation of fractures of the femoral condyles. This seems to offer superior results to all other methods of treatment.

FRACTURES OF THE FEMORAL CONDYLES have always been considered difficult ones to reduce and to maintain, regardless of whether they were simple or comminuted, supracondylar or intercondylar "T" or "Y" types. The posterior rotation of the short distal fragment has been difficult to overcome, if at all, by manipulation or traction, and when, as is occasionally the case, the sharp distal end of the proximal fragment is driven into and impaled upon the quadriceps apparatus closed reduction may be impossible. The comminution of the condyles may be so marked as to seem incapable of restoration. This type of fracture is also complicated by a rather high frequency of delayed and nonunion, regardless of the treatment method utilized. Finally, marked limitation in the motion of the knee joint has been an expected and accepted end-result in the majority of cases. The prognosis is so poor that one orthopedic textbook states: "Rarely is normal function secured, although motion ranging from full extension (180 degrees) to 130 to 90 degrees flexion is obtained in the majority of cases."[1] This total range of only 50 to 90 degrees of motion seems to be generally expected and accepted as the end-result.

Various forms of treatment have been advocated and are being used at the present time. Closed manipulation and the use of a cast are utilized in some cases. Skeletal traction with a pin or wire through the tibial tubercle on a Bohler-Braun splint, or with a Thomas splint and Pearson attachment, is also widely used at the present time.[2] Operative restoration has been attempted with screws, pins, wires, and plates, alone or in combination.[3,4] Altenberg and Shorkey[5] credit Hugh Thompson with first using, in 1943, a Moore-Blount blade plate for fixation of this type of fracture. This was followed by a report, in 1948, by Umansky[6] using the same type of fixation; in the same year Wright[7] used an original design of a blade plate of his own. Rush pins have been used by many surgeons, and many variations of external bar skeletal fixation have been tried.[4,8]

The results of the various forms of treatment as above have been rather similar, despite the different approaches and methods used. The hospital stay has been prolonged, especially with the use of traction. A high incidence of delayed and nonunion has occurred, with the nonunion always occurring in the supracondylar area due to inability to prevent excessive motion at this level.[9] These nonunions are almost always mechanical failures, rather than circulatory failures. The one feature common to all forms of treatment has been the prolonged immobilization of the knee joint, so that permanent limitation of motion and function of the knee joint has resulted in practically all cases. Too often the stiffened knee has been attributed to the type and severity of the initial fracture, rather than a proper realization that it was the result of the prolonged immobilization.

In 1952, I approached this problem by designing a new type of femoral condyle blade plate. The previous use of the Moore blade plate in the knee region left much to be desired. Extensive rebending and reshaping of the Moore blade plate was required in every case to fit the knee condyles, resulting in some weakening of the metal. Furthermore, the Moore blade plate was designed for the hip and did not satisfactorily meet the problems of the knee. At the hip, with absorption of the femoral neck, the fragments would slide together on the blade portion maintaining contact-compression, whereas when used

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fiftieth Annual Meeting, Washington, D. C., November 12-15, 1956.

at the knee the absorption and delayed and nonunions occur in the supracondylar region where the Moore plate portion is rigidly fixed to the bone with screws, preventing reapposition of the bone ends and contact-compression forces from acting. The blade portion in the cancellous bone of the condyles did not adequately control the distal femoral fragment or fragments, with their multiphase angulation, rotation, and torque stress and strain. The Moore blade plate would "cut-out" and would "halo" or loosen in the soft cancellous bone unless protected by prolonged bed rest, traction, or plaster.

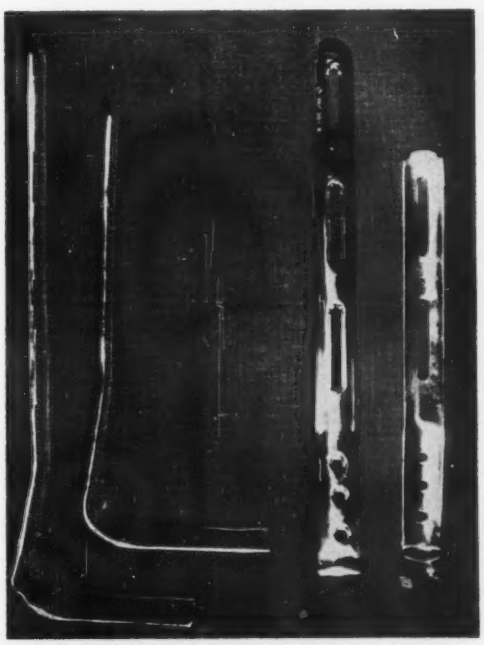
With these disadvantages in mind I designed a new femoral condyle blade plate (Fig. 1) preshaped to fit the lateral condylar and shaft surfaces of the femur, with a blade design of an inverted "V" form similar to that of the Neufeld nail plate, and with the plate portion slotted to utilize the contact-compression principles of the Eggers splint. The inverted "V" design of the blade offers better contact with the cancellous bone of the condyles and is directly opposed to the arc strain of knee motion on the condyles, as well as being mechanically better opposed to the rotational, torsional, and bending stresses and strains in this region. At the condylar bend portion of the blade plate are located three holes for additional fixation, if needed, of the distal condylar fragments with long bone screws or a Webb tibial bolt with nuts and washers, especially useful in comminuted "T" and "Y" types of fractures. The slotted plate allows continuing apposition of the fragments, if absorption occurs in the supracondylar region, and for contact-compression at all times with muscle pull in the axial line in these locations of the supracondylar fracture line. The plate is manufactured in four sizes (Fig. 1), with 6 inch and 8 inch plates, and with 3 inch and 2½ inch blades, in combinations.

During the past three years the femoral condyle blade plate has received extensive trial by me and my colleagues in private and charity cases at the local hospitals, and by Dr. G. W. N. Eggers and his associates at the University of Texas Medical School at Galveston.

Clinical Trial

The results and experiences of this trial are the substance of this paper, reporting the use of this blade plate 20 times in 19 patients with all types of supracondylar and intracondylar fractures. We have follow-up studies on 17 knees in 16 of these patients, representing 84.2 per cent. The shortest follow-up time in this series is 5 months, and the longest period is 30 months, the average being 15.2 months. The 19 patients represented 10 males and 9 females. The right femur was involved in 10 instances and the left femur in 10. The average age of the group was 47.9 years, the youngest patient being 19 and the oldest 85 years old. The distribution of cases by decades of life was as follows: second decade, 1 case; third, 3; fourth, 3; fifth, 4; sixth, 2; seventh, 4; and one case each in the eighth and ninth decades. In 12 cases (63.2 per cent) automobile accidents and collisions were the cause of the fracture, while falls and other injuries were the cause in 7 cases (36.8 per cent).

FIG. 1



The femoral condyle blade plate consists of the inverted "v" blade, the slotted portion of the plate, and three holes for additional condylar fixation if needed, and is made in four sizes. The one on the left is an 8″ plate with a 2½″ blade, the next is a 6″ plate with a 3″ blade, the next is an 8″ plate with a 3″ blade, and the last to the right is a 6″ plate with a 2½″ blade. It is recommended that two screws be placed in each slot, in such position that distraction is prevented but coaptation is allowed.

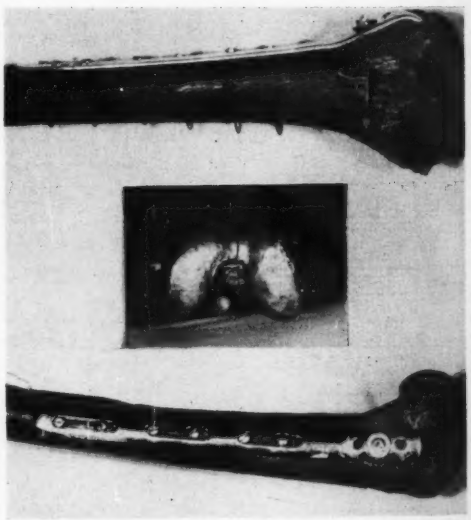
The average hospital stay for all cases, private and charity, was 35.2 days, whereas for the private patients only the average was 16.3 days. The patients of the series were unselected and consecutive, and included all ages, types and problems of femoral condyle fractures. Two cases with bilateral involvement were included, the blade plate being used on both sides in one case, and on one side only in the other case, with management by traction and cast on the opposite side as a control. Two cases of previous fracture with supracondylar nonunion were operated upon, grafted with bone, and fixed with the blade plate. The blade plate was used in one paraplegic patient who had a comminuted "T" type of fracture. Osteoarthritis was a common feature in most of the fractures in the middle and older age groups. The treatment was carried out in both private and charity hospitals, and the operations were done by me, by other Board men, by non-Board men, and to a great extent by residents in training both at Houston and at Galveston, both supervised and unsupervised.

Technic

The blade plate is applied through an anterolateral approach to the femur and condyles, consisting of a lateral parapatellar incision at the knee and extending proximally up the thigh in an anterolateral plane. The deep fascia is opened in line with the skin incision, and the quadriceps apparatus is identified. The vastus lateralis muscle is separated from the rectus femoris by blunt dissection above and sharp dissection below, removing it from its attachment to the patella, leaving about one-fourth to one-half inch of soft tissue attachments for later suture back to the patella. The knee joint is opened through the routine lateral parapatellar incision. The rectus femoris and vastus lateralis muscles are separated to expose the vastus intermedius muscle, which presents as a glistening white surface; this is split by incising in a longitudinal plane, down through the periosteum of the shaft of the femur. The periosteum and split halves of the vastus intermedius are then separated medially and laterally and exposure of the entire distal shaft of the femur is thus obtained. Upon opening of the capsule of the knee joint in the lateral parapatellar plane and dislocation of the patella medially, the entire distal end of the femur and the condyles is well visualized.

The fractured condyles are restored anatomically by fitting the fragments together, with special attention to the joint articular surfaces, and the condyles are then lined up with the shaft. The femoral condyle blade plate is placed in position, lined up properly and driven into place with hammer or mallet. No special driver is required, nor is any guide pin or x-ray control necessary, since the whole procedure is done under wide direct vision. It should be noted that the blade is inserted in the condyles in the axial line of the femoral shaft, which lies anterior to the center point of the condyles proper. The plate is then fastened to the femoral shaft with bone screws after checking the position and alignment. Additional fixation of the condyles to the blade plate is usually indicated and recommended, and can be obtained by insertion of bone screws through the three holes in the plate for that purpose, or by the use of a Webb tibial bolt with nuts and washers on each end. This latter is especially useful for additional support and fixation as well as helping to gather the pieces together in

FIG. 2



A markedly comminuted "T" type of fracture with another fracture line through the lower femoral shaft is shown in this gross specimen. The fragments are reduced and held with the femoral condyle blade plate together with a Webb tibial bolt for additional fixation of the condyles. Note in the lateral view that the blade plate is driven into the condyles in line with the vertical axis of the femoral shaft so that the point of entry into the condyles lies anterior to the true center of the condyles.

the comminuted intracondylar "T" and "Y" types. Figure 2 shows the plate applied to a fractured femur gross specimen with a Webb tibial bolt for additional fixation. This figure shows the placement of the blade plate in relationship to the fracture and also in respect to the anatomy of the shaft and condyles. Routine closure is then done in layers in the usual careful manner, compression dressings are applied; postoperatively the extremity is placed in a balanced suspension on a Thomas splint with a Pearson attachment.

Postoperatively, the patient is encouraged to start knee motion at once, particularly with quadriceps exercises. In about 7 to 14 days, when the swelling and pain have subsided, the patient is allowed up on crutches, without weight bearing on the fractured side, but with active early motion of the knee encouraged. The cases will have different degrees of comminution, and of stability following the operative procedure, so the aftercare will be varied somewhat with the individual case. We have tried to avoid splinting with plaster and immobilization for the most part, and where it has been used by some of the surgeons it has been left on only for about 4 or 5 weeks at the most. I have not used plaster on any of my patients or on those under my supervision.

The institution of early knee motion has been an integral part of our treatment. Paper after paper published from 10 to 30 years ago described the stiff knees resulting from traction and treatment in plaster of fractures of the hip, the femoral shaft, the tibial shaft and ankle.[10-13] Immobilization for prolonged periods of time will cause permanent stiffening of even normal knee joints; with actual damage to and around the knee joint proper in supracondylar and intracondylar fractures the harm and danger of plaster casts and of traction becomes even more pernicious. It is my belief that the permanent loss of motion of the knee joint as described in the past is only partly due to the initial damage, and is mainly due to the harmful treatment of prolonged traction and/or immobilization by plaster cast allowing matting of the soft tissues and the formation of extensive adhesions. Better fixation of fractures by the new blade plate has permitted us to start early and active knee motion, and seems to prevent adhesions in and around the knee joint proper and soft tissue "freezing" and "matting."

Results

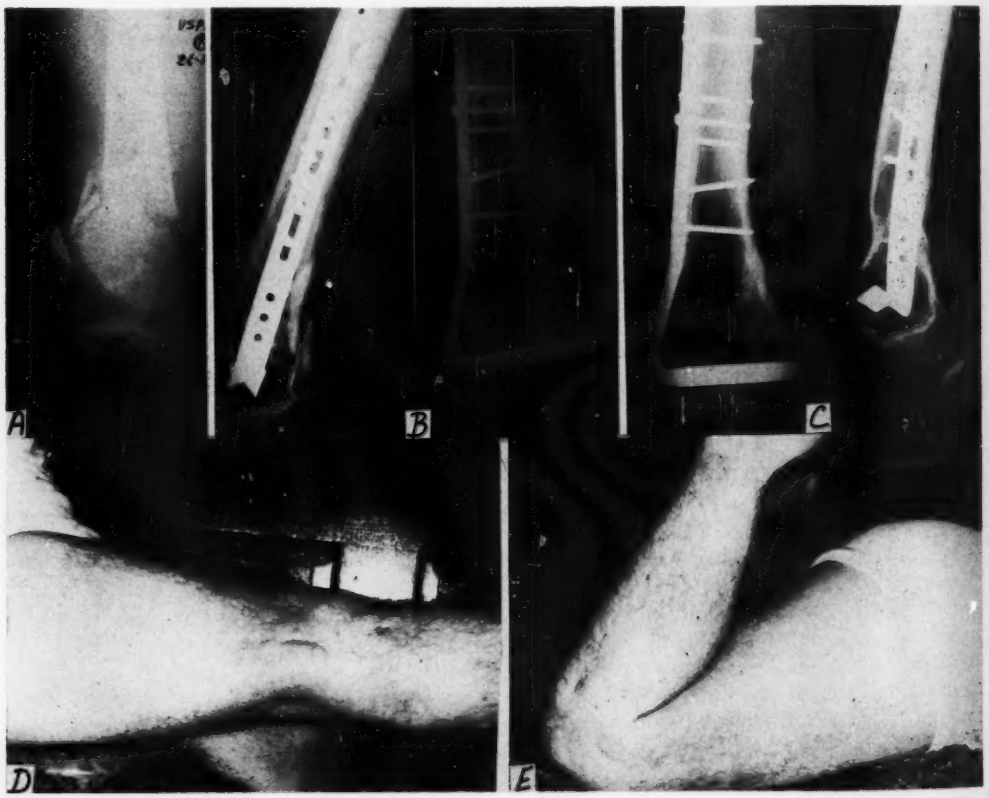
Our results in the 17 knees available for follow-up can be summarized as follows. All fractures healed without infections. Nonunion did not occur in any case in this series. Although it is impossible to determine or to prove in a study of this type, it is our impression that bone union proceeded at a slightly faster rate in most of our cases than was true with other methods of treatment used previously. The most striking result in this series of cases is the range of knee motion which is retained. The average range of active knee motion in the entire group, including the previous cases of nonunion, the paraplegic patient and the arthritics, was 111.4 degrees total motion range. In the 13 cases of fresh fractures, the average range of active knee motion was 119.0 degrees at this time. Many of the cases (Cases 1, 4, 7 [bilateral], 9 and 16) had an end-result of full 180 degree extension and practically complete flexion, as compared to their opposite knee, regardless of the type or severity of the fracture.

Only one patient failed to obtain flexion to, or past a right angle (90 degrees), excluding one patient with limited motion of the knee as the result of an old bilateral tibial plateau fracture sustained some years prior to the oblique supracondylar fracture which was treated as one in this series (Case 5). This patient had slight improvement in his final total range of motion; according to the patient,—"slightly better than I had before I broke my leg this last time." The one patient with normal knee motion prior to the fracture (Case 3), and who failed to obtain flexion to a right angle was a 67 year old white woman with generalized osteoarthritis of moderate degree. She was able to extend the knee to 180 degrees and flex it to 100 degrees, giving a motion range of 80 degrees in all.

Only 7 patients failed to obtain 180 degrees of active extension of their knees. Two of these had never had 180 degrees of extension to begin with; one (Case 13) was 85 years old and had mild old age flexion contractures of both knees prior to the fracture. The other

case (Case 5) has been discussed above, that of the man who had the previous tibial plateau fracture with loss of the final 10 degrees of extension prior to this injury. Of the remaining 5 cases, 2 patients (Cases 2 and 12) extend the knees to 176 and 175 degrees respectively, and it is hoped they will eventually regain 180 degrees extension with further time, exercise, and use. The third patient (Case 10) extends the knee to 164 degrees; this is the one having bilateral fractures, the opposite knee having been treated with traction and casts as a control resulting in only 155 degrees of extension. She is only 12 months postoperative and still improving, her course having been complicated by two operations for kidney stones during this interval. The fourth case (Case 11), is that of a 69 year old arthritic, whose knee was operated upon previously because of the arthritis, with debridement of the joint and insertion of a patellar prosthesis elsewhere, who extends the knee 157 degrees. She stated that she lacked complete extension of this knee prior to the fall which produced a comminuted supracondylar type of fracture in this knee. The femoral condyle blade plate in this case was erroneously inserted on the medial side of the femur through an anteromedial operative approach, and was also complicated by a fall onto this knee on the tenth postoperative day, causing slight angulation of the condyles to the shaft and impacting them onto the shaft. Nevertheless she extends the knee 157 degrees actively (180 passively), and flexes to 15 degrees past 90, an active range of motion of 82 degrees. The fifth patient (Case 14) extends the knee only 158 degrees but is only 6 months postoperative and still improving. He has had no physio-

FIG. 3, A-E



Case 1. Comminuted supracondylar fracture. (A) Preoperative. (B) Postoperative, showing reduction. (C) Thirty months later. (D) Full 180 degree extension present at 30 months. (E) Amount of flexion lost can be measured by comparing the two heels.

therapy, is still using crutches despite solid bony union as shown by x-ray examination, and is under the care of another doctor elsewhere. He is expected to improve with further time, exercises, and use of the leg.

Summary

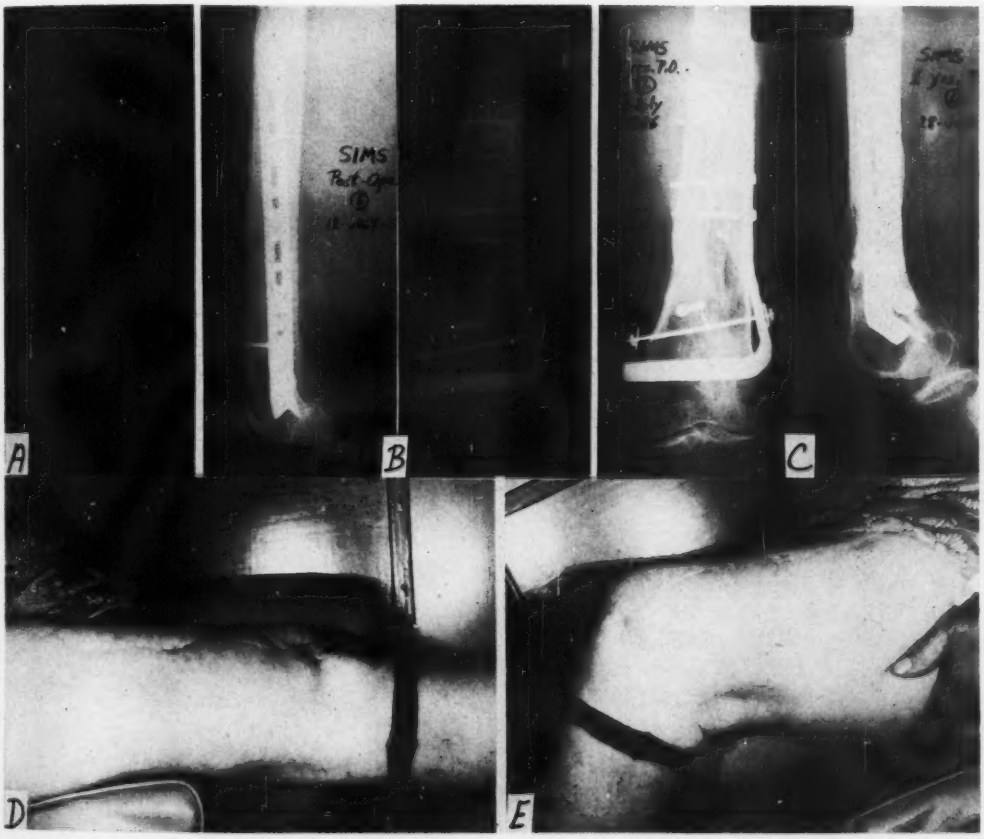
A femoral condyle blade plate of new design has received extensive testing during the past three years by several surgeons under varied circumstances on all types of fractures of the femoral condyles. No nonunion has occurred, and we believe that a slightly faster healing time has prevailed. A better end-result, in terms of motion of the knee joint has been demonstrated in the whole series. Many of the patients, about one-third of the series, have practically normal knees. These results are attributed to the anatomic restoration of the knee joint, and to the early institution of active motion of the knee joint by avoiding plaster casts and traction, as permitted by this blade plate design with its better fixation and multiple functional advantages.

Case Reports

Case 1. (Courtesy of Dr. William Etheridge, U.S.P.H.S., Galveston) A. R., a 24 year old white man, had a comminuted oblique supracondylar fracture of the right femur in a fall on Feb. 26, 1954 (Fig. 3). Fixation with the femoral condylar blade plate on the next day was followed by balanced suspension and early active knee motion. He remained in the government hospital, ambulatory and receiving physiotherapy for a total of 142 days. Follow-up time is now 2½ yrs., with extension of 180°, flexion of 42° past 90, total range of motion 132°, the same as in opposite knee. There is no limp, pain, nor disability.

Case 2. (Courtesy of Dr. E. J. Tucker, Houston)

FIG. 4, A-E



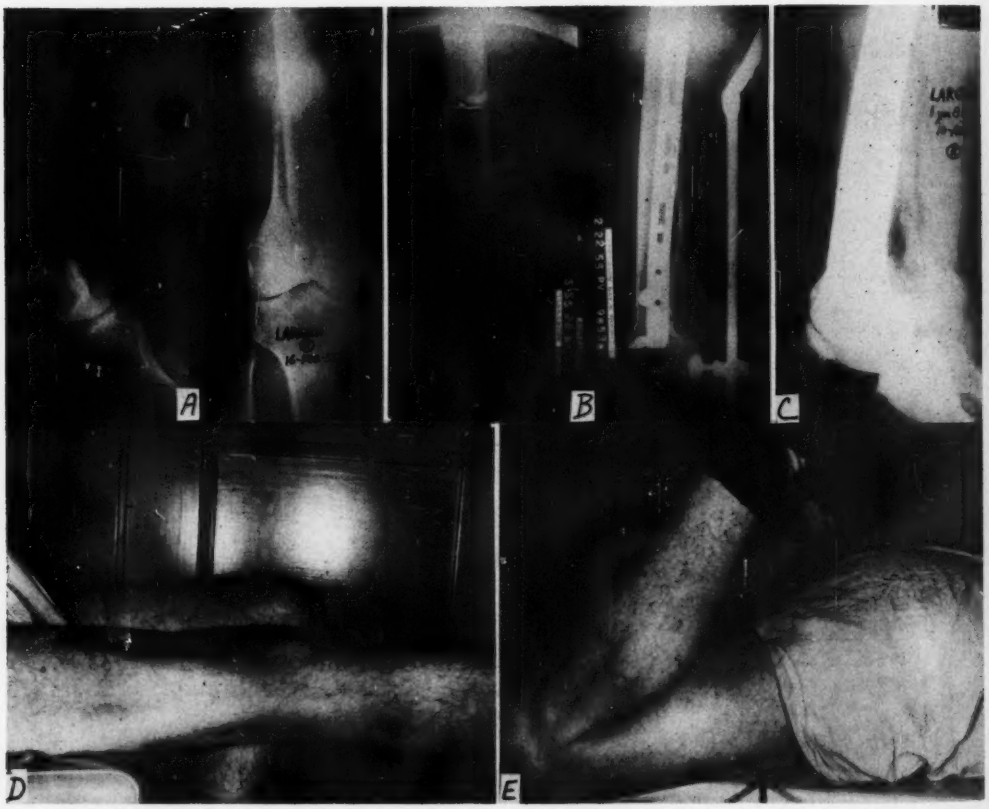
Case 3. (A) Shows fracture. (B) Postoperative, shows reduction and fixation. (C) Two years postoperative. (D) Extension 2 years postoperative. (E) Flexion.

B. B., a 71 year old white woman, sustained a very low transverse supracondylar fracture of the right femur in a fall on Jan. 31, 1954. She was very obese, and previously had received treatment for severe osteoarthritis in both knees. Fixation with the blade plate was done 2 days after injury with fair reduction. Postoperatively the leg was placed flat in bed. The hospital stay was only 9 days, patient returning to her home town and receiving little postoperative care and no physiotherapy. Follow-up time is now 2 yrs. and 7 mos., with extension of 176°, flexion of 44° past 90, total range of motion 130° (129° total motion in opposite normal knee). There is no pain, aching, nor barometric sensitivity.

Case 3. J. B. S., a 67 year old white woman, sustained a comminuted "Y" type fracture of the left femur on July 9, 1954, in an auto accident. There was also a fracture of the tibial condyles, with minimal displacement, of the opposite knee (Fig. 4). She had severe generalized symptomatic osteoarthritis prior to injury. Three days after injury a blade plate was inserted and the leg placed flat on bed postoperatively. The hospital stay was 19 days. At follow-up 2 years later, extension was 180°, flexion 100°, with a total knee motion range of 80°. She is satisfied with the knee and not interested in gaining further motion. There is no limp nor pain, and it bothers her less with changes in weather than the opposite one does. (This is the only case in the series in which there was "normal" knee motion prior to the fracture and in which flexion to at least a right angle or more was not obtained.)

Case 4. T. J. L., a 44 year old white man, sustained a comminuted "Y" type fracture of the right femur in a fall on Feb. 17, 1955, and an incomplete, undisplaced fracture of the neck of the left radius. Operation on the knee was done 48 hours later with fixation by a blade plate, and balanced suspension postoperatively (Fig. 5). The hospital stay was 20 days. At follow-up 18 mos. later, extension was 180°, flexion 51° past 90, with a total range of motion of 141°. The range of motion was the same as in the opposite knee. There was no limp, pain, nor aching, nor sensitivity to weather. The blade plate was removed 12 weeks postoperative, on May 5, 1955, because it protruded through the medial femoral condyle and caused a local painful bursal reaction over the end of the blade. (This is one of two in the

FIG. 5, A-E



Case 4. Comminuted "Y" type of fracture. (A) Fracture. (B) Postoperative, reduction and fixation. (C) Postoperative, 20 months. (D) Full 180 degrees extension; the anterolateral approach is shown. (E) Prone with both knees in actue flexion; fractured knee is toward the camera; amount of flexion lost can be seen by comparing distance between the heels and buttocks.

series in which the blade plate was removed,—both for this same cause.)

Case 5. C. L. S., a 36 year old white man, sustained an oblique step-type supracondylar fracture of the right femur in an auto accident on March 5, 1955. He had had a severe fracture of both tibial condyles in this same knee several years previously, at which time elevation of the tibial plateaus, bone grafting, and fixation with three large lag screws were done at open reduction. His knee had very limited motion prior to the supracondylar fracture. Skeletal traction for 10 days did not obtain reduction, whereupon fixation by blade plate was done, followed by balanced suspension and early knee motion. Total hospital stay was 21 days. At follow-up 17 mos. later, extension was 180°, flexion 15° short of 90 and total range of motion was 65°. This patient says the motion in the knee is about the same or perhaps "a little bit better than it was" prior to this last fracture. There is no pain nor aching. He was lost to follow-up following his dismissal from the hospital and received no postoperative care. Later he stated that 1 month postoperatively, he discarded his crutches, walking without them, and by 2 months postoperative he had roofed two houses.

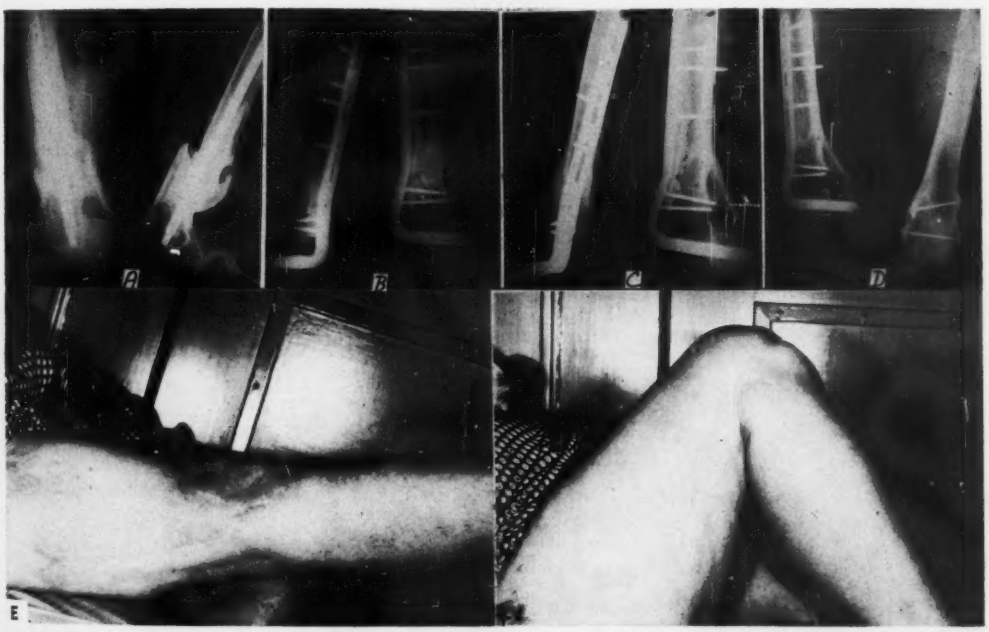
This can only be explained by the fact that his fracture was of a step-type oblique supracondylar one with strong fixation by the blade plate; he must have had an abundant early healing reaction, plus an unprecedented amount of blind good luck.

Case 6. L. R. H., a 52 year old white woman, originally had comminuted supracondylar fractures of both femurs resulting from an auto collision in December, 1953. The left femur was reduced openly and fastened with bone screws, lag screws, and a threaded bolt with washers and nuts on each end, and with immobilization by plaster cast. This left femur proceeded to solid union.

The right femur was of a high supracondylar type, and was reduced surgically, held with an intramedullary femoral rod driven very low into the condyles. She was in a plaster spica cast for 6 months, and then in a leg brace and on crutches.

She was first seen at Galveston 16 months after the injury because of marked nonunion of the right femur (Fig. 6). On April 11, 1955, at operation the intramedullary rod was removed, the area of nonunion was freshened, shortening the femur slightly to approximate bleeding bone ends, autogenous cancellous bone grafts were applied and fixation obtained with a femoral condyle blade plate. Postoperatively she was placed in balanced suspension, and then in a plaster cylinder cast which was worn for about 6 weeks. Hospital stay postoperatively was 14 days. At follow-up 16 months later there was solid union, extension of 180°, flexion of 24° past 90, and a total range of motion of 114°. The right leg is one and a quarter inches shorter than the left, secondary to the absorption, nonunion and shortening at the time of the operation. There is no pain nor aching. She claims the

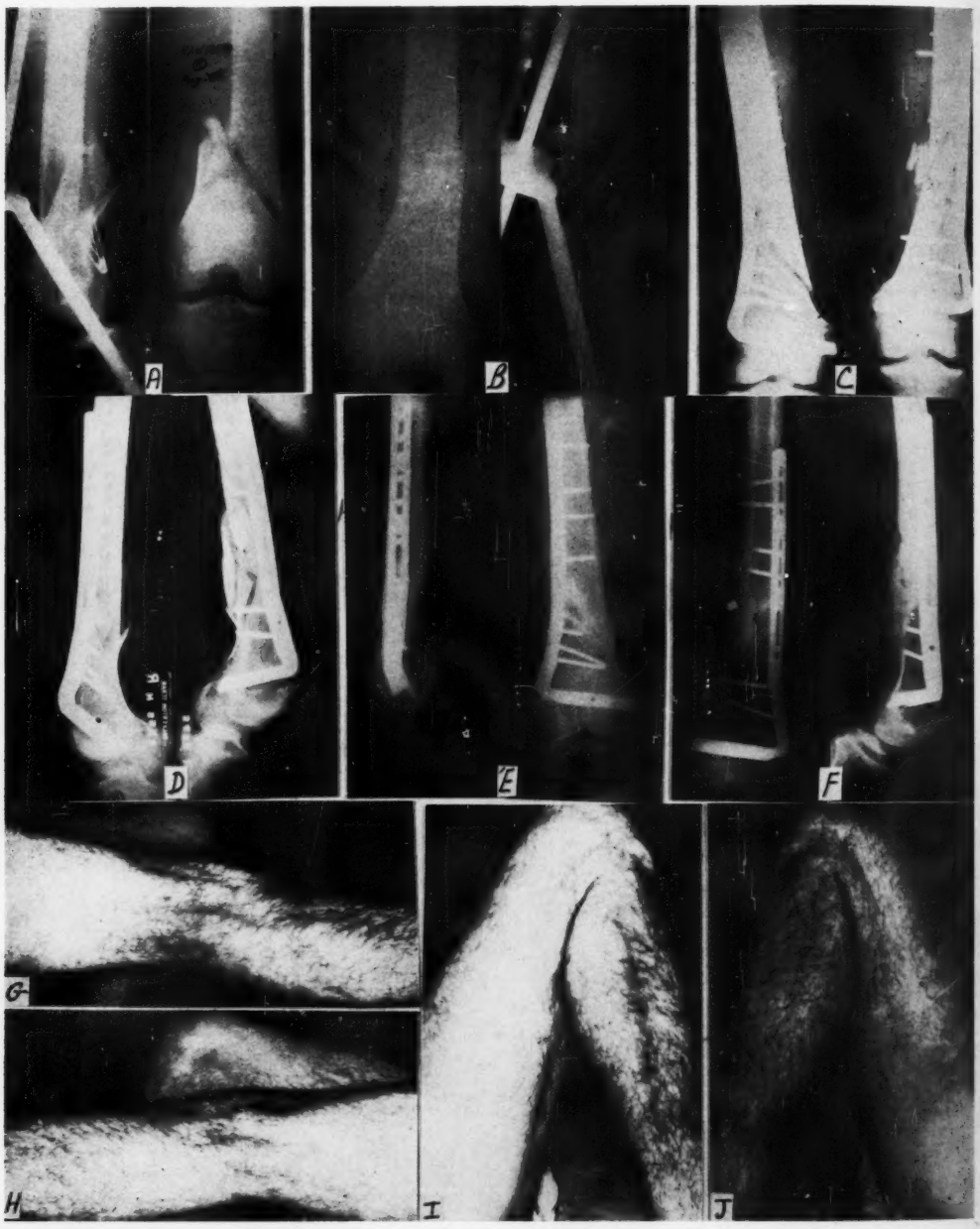
FIG. 6, A-F



Case 6. Nonunion in a supracondylar fracture. (A) Nonunion of 16 months duration. (B) Postoperatively, reduction and fixation, and bone grafting in treatment of the nonunion. Note the imperfect reduction. (C) Postoperative, 16 months. (D) Postoperative, 16 months. Both femurs compared. Solid union now present in the right femur; shortening done at surgery is shown. (E) At 16 months showing full 180 degree extension. Operative scar shows a posterolateral approach was tried, but did not adequately expose the condyles and contributed to the poor reduction and alignment. (F) Flexion present at 16 months, measuring 24 degrees past 90.

right knee is much stronger and better than the left; she has approximately the same range of motion in both knees despite the fact that the right knee had two operative procedures and was in very unstable nonunion for over a year before the second operation was done.

FIG. 7, A-J



Case 7. Bilateral fractures. (A) Right femur, note failure of traction. (B) Left femur, note failure of traction. (C) Postoperative, AP view of both femurs. (D) Postoperative, lateral view of both femurs. (E) Right femur, showing union present at 16 months. (F) Left femur, showing union present at 16 months. (G) Right knee, showing extension. (H) Left knee, showing extension. (I) Right knee, showing flexion. (J) Left knee, showing flexion.

FIG. 7, K

Patient with knees flexed.

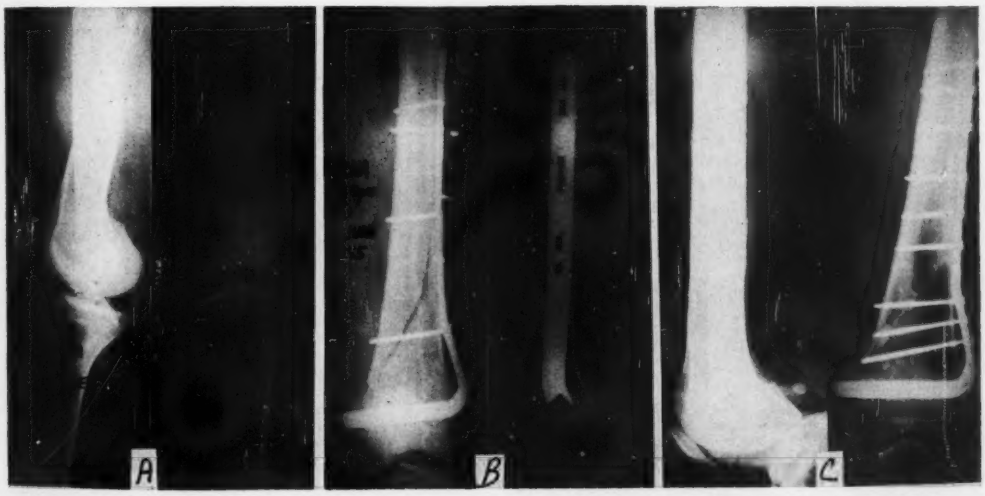
Case 7. F. A. C., a 27 year old white man, sustained bilateral supracondylar fractures of both femurs on March 30, 1955, when a log fell across both knees (Fig. 7). Conventional skeletal traction on both knees for 2 weeks failed to obtain satisfactory reduction of either fracture. The left knee was operated upon on April 12, and the right knee on April 19, blade plate fixation being used in both knees, followed by balanced suspension postoperatively, with early active knee motion. Hospital stay was 45 days. He wore bilateral cylinder plaster casts on both legs from the dismissal date from the hospital for about 5 weeks thereafter. At follow-up at 16 months the left knee extended 180°, and flexed to 57° past 90, with a total range of 147°. The right knee extended 180°, flexed 54° past 90, with a total range of 144°. He has no limp, no pain, and no sensitivity to weather. Had been in fields gathering corn when interviewed for follow-up study. (This is the only case in the series with bilateral fractures and the use of the blade plate on both sides primarily and initially.)

Case 8. (Courtesy of Dr. J. W. Jinkins, Jr., Galveston) F. E. F., a 49 year old white man, had a comminuted "T" fracture of the left femur in a fall on June 4, 1955. The past history revealed he had been partially paralyzed in both legs for 22 years. The right was worse than the left, and he walked only with a cane. He attributed this paralysis to "polio." The reflexes were hyperactive in both legs, with muscular spasticity, the right worse than the left. The final diagnosis was spastic paraplegia, onset at age 27, type and cause undetermined. The fracture was treated by fixation with a femoral condyle blade plate 4 days after injury and a posterior plaster leg splint. Hospital stay was 11 days. At follow-up time at 14 mos., extension 180°, flexion actively 4° short of 90, and passively knee bends 32° past 90, with total range at the knee of 86° actively and 122° passively. This left leg was and is still his better leg, and he is walking with the aid of a cane as before.

Case 9. J. R., a 27 year old Mexican man, sustained a comminuted "T" type fracture of the left femur on June 25, 1955, in an auto accident (Fig. 8). Associated injuries included a fracture of the right iliac bone, the left humeral shaft, the right ulnar shaft, and a trimalleolar fracture of the right ankle.

The femoral fracture was fixed with a condyle blade plate, followed by balanced suspension on June 28. Hospital stay was 23 days; a cylinder cast was worn for about 6 wks., and crutches were permitted 3 mos. postoperatively. At follow-up time at 14 mos. extension is 180°, flexion 46° past 90, with a total range of 136°. (About 10° less than the opposite knee.) There is no pain nor limp, though he has slight sensitivity to weather.

FIG. 8, A-C



Case 9. Oblique supracondylar and intracondylar mixed type of fracture. (A) Fracture. (B) Postoperative, reduction and fixation. (C) Postoperative, 14 months showing the union. Note the blade plate protrudes through the medial cortex of the femoral condyle.

The end of the blade protrudes through the medial femoral condyle and can be palpated on the medial aspect of the knee joint with slight local tenderness present. However, it does not bother the patient sufficiently to have it removed, as recommended. He is working as a cement finisher, a job which requires working on both hands and knees with full flexion in both knees.

Case 10. H. J., a 32 year old white woman, sustained bilateral femoral fractures on August 13, 1955, in an auto collision (Fig. 9). The fracture of the right femur was a compounded comminuted supracondylar type, and was treated with primary debridement and closure, followed by skeletal traction with a tibial tubercle pin initially, and with a long leg plaster cast. Subsequently Steinmann pins were inserted high into the femoral shaft and incorporated into the plaster cast for fixation and immobilization.

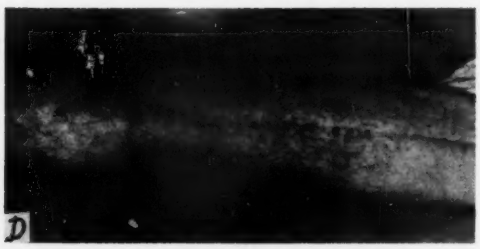
The fracture of the left femur was a comminuted "T" type and was fixed 2 days after injury with a femoral condyle blade plate, and with balanced suspension and active motion exercises postoperatively. Hospital stay was 42 days.

Three months postoperatively hospitalization was necessary because of pyelonephritis and renal lithiasis, requiring surgical treatment and a 60 day hospital stay. Three months later another acute episode of pyelonephritis was treated medically. No further treatment for the knee nor physiotherapy were given, either as an in- or out-patient.

The follow-up at 1 yr. was in the patient's back yard, where she was walking with a fair gait, stiffly, and with a cane (August 25, 1956). The right supracondylar fracture which had been treated with a cast showed extension of 155°, and flexed 20° short of 90, with a total range of 45°. The left knee, with the comminuted "T" fracture treated with the blade plate, extended 164°, flexed 20° past 90, and had a total range of 94°. Since she was last seen at the hospital she had more or less stayed in bed and in a wheel chair, and had been trying to walk for only about the past 2 mos. The right knee was stiffer, felt stronger to her, and had no pain in it. The left knee had more motion and seemed to be improving slowly week by week. She was quite small and thin and complained of tenderness over the metal plate in the left leg, with some consciousness of the weather.

In this case of bilateral fracture, without any follow-up care, the more severe fracture on the left shows almost double the motion of the right and seems to still be improving.

FIG. 8, D



Extension present at 14 months.

FIG. 8, E

Flexion present at 14 months. Lateral operative approach was found to be less desirable than the anterolateral one.

Case 11. (Courtesy of Dr. Duncan C. McKeever, Houston) E. C., a 69 year old white woman, had a comminuted supracondylar fracture of the left femur in a fall on Oct. 18, 1955. Past history revealed that she had had an operation on this knee on May 14, 1953, for severe disabling arthritis, with surgical debridement of the knee joint, removal of both semilunar cartilages, and insertion of a patellar prosthesis. The subsequent course was good until the fracture occurred.

On the day after the injury, through an anteromedial approach, the blade plate was inserted on the medial aspect of the condyles and shaft rather than on the lateral, as usual. Bone grafts were also placed about the fracture and a cellophane sheet was placed between the quadriceps apparatus and the bone. Hospital stay was 14 days.

Follow-up examination at 10 mos. showed extension of 157° actively, and 180° passively. The difference is thought due to lack of quadriceps tone and strength, particularly of the vastus medialis. Flexion was 15° past 90, a total range of 82° actively, and 105° passively. She says the knee seems to get stiff with sitting and inactivity, and is sensitive to weather. She is working as a corsettiere in a local department store. The knee seems to continue improving.

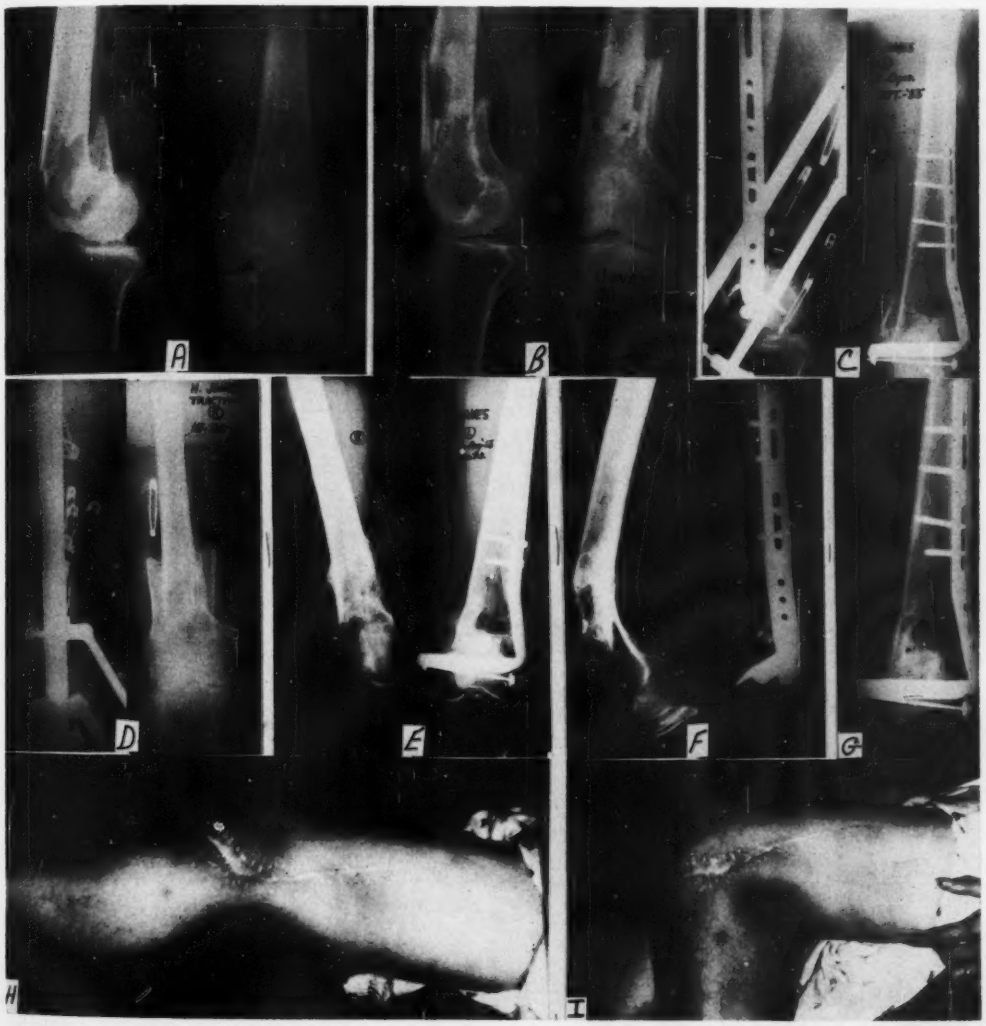
The convalescence in the hospital was complicated by a fall on the treated knee on the 7th postoperative day, which caused slight angulation of the condyles to the shaft, and telescoped and impacted the condyles and the distal end of the shaft of the femur. Apparently no permanent harmful effects occurred from this fall. Quadriceps exercises are indicated, but she will not carry them out. Further improvement is expected in the active range of motion with additional

time and use. (She is the only patient in whom the blade plate was inserted on the medial condyle side, and the only one who fell on the fractured limb early in convalescence.)

Case 12. M. A. P., a 65 year old Negro, had a severely comminuted oblique supracondylar fracture of the left femur on July 30, 1955, when a bale of hay fell off a wagon and on his leg. Fixation with a condyle blade plate was done on the same day. Balanced suspension was used postoperatively until the 10th day when a cylinder plaster cast was applied,—this was worn for 3 mos. because the patient did not return, as requested, for removal and follow-up. Hospital stay was 11 days. Follow-up examination at 13 mos. showed extension of 175°, flexion of 19° past 90, and a total range of 104°. He is working as a farm laborer. The knee occasionally aches and pains, especially with changes in weather and excessive activity. (The plaster immobilization was carried out much longer than was necessary and there was no physiotherapy, because of the patient's lack of cooperation, which gave a poorer end-result than might otherwise have been obtained.)

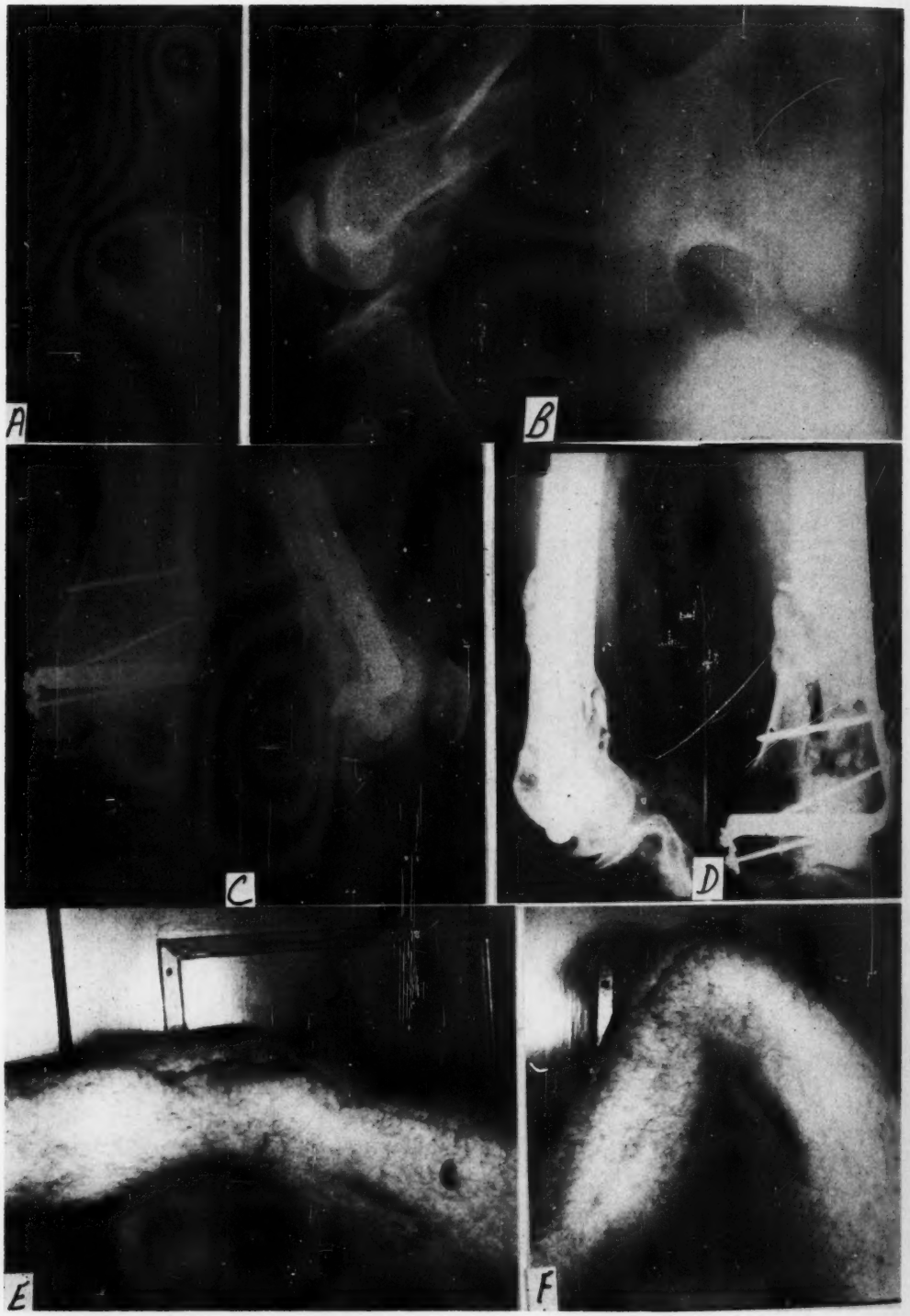
Case 13. M. R., an 85 year old negress, sustained

FIG. 9, A-I



Case 10. A bilateral supracondylar fracture. The blade plate was used in the worst knee, and conventional traction and cast used in the other knee for control comparison. (A) Fracture of left knee. (B) Fracture of the right knee. (C) Postopreative, left knee, the femoral condyle blade plate in place; poor reduction obtained. (D) Right knee in conventional traction. (E) Postoperative, 1 year, AP view of both femurs, with union present in both. (F) Lateral view, right femur at 1 year. (G) Left femur at 1 year. (H) Extension, both knees at 1 year. (I) Flexion, both knees at 1 year. There is increased flexion in the knee which was operated upon as compared to that treated by conventional traction and plaster cast.

FIG. 10, A-F



Case 14. Severely comminuted "T" type fracture. (A) Fracture. (B) Note failure of conventional traction to reduce the fracture (lateral view). AP view shows the intercondylar portion of the fracture and supracondylar comminution present. (C) Postoperative, reduction obtained and technic of fixation with Webb tibial bolts used in addition to the condyle blade plate. (D) Postoperative, at 6 months. (E) Postoperative, extension at 6 months. (F) Postoperative, flexion at 6 months.

a comminuted supracondylar fracture of the left femur in an auto accident on Oct. 30, 1955. A femoral condyle blade plate was inserted on Nov. 9. The reduction was poor and the placement of the plate was only fair, due to hurried surgery because of the patient's condition during the anesthesia and operation. She was placed in balanced suspension postoperatively with active exercises of the knee begun immediately. She developed a decubitus ulcer on the opposite heel which required debridement and skin grafting. Therefore, her hospital stay was 70 days.

At follow-up at 10 mos. extension was 178°, flexion 20° past 90, and a total range of 108° (129° total range in opposite normal knee). The patient is very active with solid union and walks without any limp; there is no pain or tenderness except occasionally aching in the joint with activity and weather changes. (This is the oldest patient in the series, and attained this 10 mo. end-result despite poor reduction of the fracture and only fair placement of the blade plate.)

Case 14. J. E., a 38 year old white man, had a severely comminuted mixed "T" and supracondylar fracture of the left femur in an auto collision on Jan. 26, 1956 (Fig. 10). Sixteen days in skeletal traction in a Thomas splint and Pearson attachment failed to reduce the fractures. Insertion of a condyle blade plate and Webb tibial bolt across the condyles was done on Feb. 11. Balanced suspension was used postoperatively. Hospital stay was 33 days (16 days in traction, 17 days postoperatively).

He then disappeared from our care until he was located 6 mos. postoperatively for follow-up examination. Then he was still on crutches, bearing no weight on the fractured limb, had not been instructed in any knee exercises, and had had no physiotherapy. The quadriceps were very weak; he protected the knee constantly. Extension was 158°, flexion 32° past 90, and total range 100°. He was instructed in proper quadriceps exercises and limbering-up exercises, weight bearing, and other measures, and advised to return to his attending (?) doctor for continued care. (We feel if he carries out the exercises he will regain most, if not all, of full extension, and with the flexion already present, will have a very good result.)

FIG. 11, A-E

Case 16. Low femoral shaft fracture. (A) There was failure of reduction by conventional traction. (B) Postoperative, reduction and fixation. There has been poor placement of the blade portion of the plate, its end protruding through the medial femoral condyle posteriorly. (C) At 3½ months the blade plate was removed. Note union present. (D) Postoperative, 5½ months, AP views of both femurs on one film for comparison. Note that the horizontal plane of the femoral articular surfaces has been maintained in relationship to the vertical axis of the femoral shafts. (E) At 5½ months union is present.

Case 15. (Courtesy of Dr. J. W. Jinkins, Jr., Galveston) L. N., a 66 year old white woman, sustained a comminuted "Y" type of fracture of the right femur in an auto collision on March 14, 1956. Conventional skeletal traction for 2 wks. failed to reduce the fracture. A condyle blade plate was inserted on March 28, with balanced suspension afterwards. Hospital stay was 29 days (14 days in traction, 15 days postoperatively). At 5½ mos. she had been walking for about 7 wks. in a walker, and about 4 wks. without aids. She still had a slight limp in the right leg, but no pain nor sensitivity to weather, although the opposite knee does bother her some with changes in weather. The knee extends to 180°, flexes to 90°, with a total range of 90°. (It is felt she will gain further motion in flexion with more time and activity, and that the present result does not indicate the final status.)

Case 16. (Courtesy of Dr. J. W. Jinkins, Jr., Galveston) J. J., a 19 year old Negro, sustained a simple oblique high supracondylar (or very low femoral shaft) fracture of the right femur in an auto accident on April 9, 1956 (Fig. 11). Associated injuries included a fractured clavicle, a fractured pelvis, and a severe basilar skull fracture due to which his life hung in the balance for several days. The insertion of a condyle blade plate was done on April 19. Hospital stay was 30 days. The blade plate was removed on August 8, due to protrusion of the blade through the medial femoral condyle cortex (the blade was too long in our earliest pilot models) with local tenderness over its end. He was examined subsequently at 5½ mos., when solid union was present; he had a normal gait, no limp, nor pain or aching, and no sensitivity to weather. Extension was 180°, flexion 52° past 90, and total range of motion 142° (152° total range in the opposite normal knee). (This case was the youngest patient in the series, and one of the 2 in whom the blade plate was removed.)

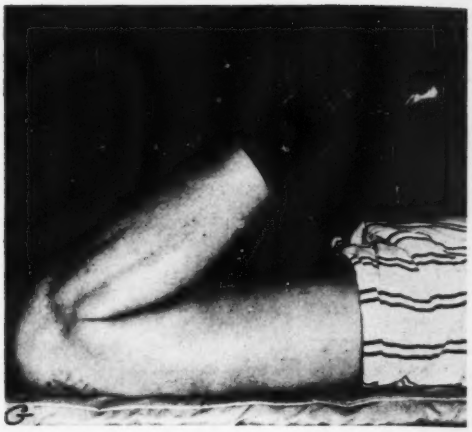
Case 17. J. H. S., a 43 year old Negro, sustained a comminuted supracondylar fracture of the right femur on Oct. 2, 1954, in an auto collision. Associated injuries included 6 fractured ribs with hemothorax. Open reduction and internal fixation was done on Oct. 13, with balanced suspension afterwards. Hospital stay was 41 days. He never returned for further care, and no follow-up examination has been possible.

Case 18. V. S. P., a 41 year old negress, had a comminuted "Y" type of fracture of the right femur in an auto accident in April, 1954; open reduction and fixation at the time with a Moore type of blade plate was followed by a supracondylar nonunion.

FIG. 11, F

Extension at 5½ months.

FIG. 11, G



Flexion at 5½ months. Compare with normal knee in the background.

The patient was admitted to John Sealy Hospital on Oct. 25, 1955. The Moore blade plate was removed, the bone ends freshened, bone grafts applied, and fixation with a femoral condyle blade plate of our design was done. Balanced suspension was used afterwards. Hospital stay was 45 days.

After dismissal from the hospital on crutches the patient failed to return. Despite our intense interest because of nonunion with another type of blade plate and subsequent bone graft and fixation with a femoral condyle type of blade plate, we have been unable to locate this patient for follow-up study.

Case 19. W. R., a 56 year old white woman, sustained a comminuted supracondylar fracture of the left femur in an auto collision on May 14, 1955. Traction failed to obtain reduction. A femoral condyle blade plate was inserted on May 27. She was extremely obese and was placed in a posterior plaster splint postoperatively, followed by a cylinder cast for 6 weeks after dismissal from the hospital. Hospital stay was 13 days. She returned for a time to the outpatient clinic and seemed to be healing well. No measurements nor range of motion were recorded. The patient disappeared and no recent follow-up examination has been possible.

Note of Appreciation

The author wishes to express his thanks and appreciation to the residents at Jefferson Davis Hospital, Houston, Tex., for their assistance in the clinical application of this femoral condyle blade plate, both supervised and unsupervised, and to the other doctors for their kind cooperation and permission in including their private cases in this study. He especially expresses his gratitude and appreciation to Dr. G. W. N. Eggers and his associates and residents at John Sealy Hospital, University of Texas Medical School, Galveston, Tex., for their cooperation and assistance in helping to test and evaluate this blade plate.

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Discussion (Abstract)

Dr. Marvin M. Gibson, Washington, D. C. Upon reviewing Dr. Elliott's paper my first reaction was an adverse one. The amount of metal adjacent to the knee joint appeared to be "hardware" rather than an "internal fixation device." However, an operative procedure that calls for immediate postoperative knee motion and early ambulation on crutches in this difficult fracture must be given careful consideration. We are all aware of the limitation of motion at the knee caused by prolonged periods of traction and/or immobilization by plaster.

Dr. Elliott's results speak quite well for themselves and cannot be equaled in the severe fractures by present conventional treatment. He is to be complimented for this series of cases and must be a native Texan because of his courage in permitting his patients to bear weight on the extremity so early after operation. I believe the author's femoral condyle blade plate will soon be looked upon as an "internal fixation device."

A question promptly raised, "is removal of the device indicated?" From the ranges of motion obtained it appears not.

I wish to present a case of nonunion in which the author's operative procedure would, I feel, be particularly indicated.

A 70 year old obese woman sustained, among other fractures, a right supracondylar fracture and a left supra- and intracondylar fracture.

Treatment consisted of skeletal traction through the tibial tubercle and balanced suspension. The right femur proceeded to union after 12 weeks of traction and 6 weeks in a long-leg cylinder cast. Traction was continued on the left for 12 weeks, and at the end of this time the intracondylar fracture had healed, but not the supracondylar fracture. Traction was then discontinued and under local anesthesia three Knowles pins were placed across the fracture site and a long-leg cylinder cast applied. Cylinder casts were continued for 15 weeks. A nonunion was present at the end of 27 weeks. An ischial weight-bearing brace was fitted and the patient has been ambulatory for 2 years. Ranges of motion in the right knee are 180 to 60°; in the left knee from 176 to 120° 30 months following injury.

New Treatment for Pruritus Ani*

CLIFFORD C. WILSON, M.D., *Kansas City, Mo.*

The author emphasizes the efficacy of the corticosteroids in the management of a distressing condition.

FIFTY YEARS AGO Sir Charles Ball,[1] Professor of Surgery at the University of Dublin, introduced the first effective treatment on record for pruritus ani. It was surgical and consisted of undercutting the perianal skin. This operation with its modifications was quite a popular treatment for those who had the courage to use a radical procedure for intractable pruritus ani. Injection of alcohol, tattooing and x-ray were also considered to be effective therapy by some. Various ointments and lotions have been prescribed, but no treatment has been universally accepted, which leads us to the statement in Ball's fifty year old textbook (1908): "At a recent meeting of the British Medical Association at Oxford an interesting discussion took place in the Section of Dermatology on the causation and treatment of pruritus ani. Anyone reading that debate cannot fail to be struck with the enormous number of distinct diseased conditions to which this annoying symptom was attributed by the various speakers. Large as the numbers of supposed causes assigned were, the various plans of treatment advocated were still greater. All the resources not only of the pharmacopeia but of the extra pharmacopeia being in turn favored."

This statement by Ball was generally true in meetings of our own dermatologists and proctologists until five years ago when hydrocortisone acetate became available and was hailed by Becker[2] as a "miracle drug." He said, "It is surely God's gift to those suffering from idiopathic pruritus ani, as well as those individuals living with and around patients suffering from pruritus ani." Time has just about proved his statement to be true. Since that statement was made we have had drugs available, or soon to be available, that are ten to twenty-five times as effective as hydrocortisone acetate, which is almost a specific for anogenital pruritus in 90% of the cases.

The types of pruritus ani which I will consider are the *mycotic, allergic* and *idiopathic* which make up 95% of the cases bringing patients to the proctologist for treatment of intractable anal or anogenital pruritus. The type case can usually be classified by the history, the appearance of the perianal skin and the laboratory findings.

In the *mycotic* type the perianal skin has a thickened scalded appearance, a long history of itching, and the area is well demarcated. The *allergic* type has a flushed appearance, poorly outlined, and is of recent origin, or flares up after taking certain drugs, food, or drink, or can be traced to contact with some chemical or type of clothing. Some patients show little or no change in the appearance of the perianal skin and these usually respond to antihistamine topical creams.

Sulzberger and associates[3] reported that of numerous dermatoses which are known to be benefited by the topical application of steroids, including fludrocortisone, the following are the most important and the most frequently encountered:

1. Allergic eczematous contact dermatitis.
2. Atopic dermatitis (including infantile eczema).
3. Intertrigo (inflammatory).
4. Nummular eczema.
5. Pruritus ani, vulvae or scroti.
6. Miscellaneous eczematous and pruritic dermatosis.

Sulzberger and associates[3] also stated that in common with its related corticosteroids, fludrocortisone in most ways fulfills the requisites of what might be called an "ideal" topical agent (if such ever exist) since: (1) it is effective in many common skin conditions; (2) it can be incorporated into several vehicles

*Read before the Section on Proctology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

(certain creams, ointments and lotions) in which it remains stable; (3) it is easy to use, is rapidly effective and the effectiveness is usually maintained as long as the medication is used regularly; (4) it is pleasant to use, and it is without stain, sting or stink; and (5) it has a low index of sensitization (thus far no cases of allergic sensitization have been reported).

Ballinger and associates[4] reported 98 patients having various dermatoses who were treated with preparations of fludrocortisone. The best results were obtained in dermatitis venenata and anogenital pruritus. Noojin[5] reported 26 of 29 patients with various pruritic dermatoses who showed decided improvement when treated with fludrocortisone.

Florinef-S* lotion and ointment is fludrocortisone acetate with neomycin and gramicidin (Spectrocin) added.

The pharmacologic action of fludrocortisone is that it inhibits inflammatory reactions to allergins, chemical, and physical irritants. This anti-inflammatory action is ten to twenty-five times that of hydrocortisone. It also has strong antipruritic action.

Noojin[5] stated that the most successful antipruritic thus far made available for topical use are hydrocortisone and its related compounds. Many reports have indicated that these agents consistently relieve pruritus in approximately four out of five patients. The one great drawback has been the expense. He also said that many dermatologists have expressed their opinion that hydrocortisone and related compounds are more effective when used locally than any other preparation hitherto available.

Recently to these improved hydrocortisone drugs (Florinef-S Cream) along with neomycin and gramicidin has been added mycostatin. Mycostatin is a fungicide, and neomycin and gramicidin are antibiotics which are effective against a pyogenic superimposed infection. There are many hydrocortisone preparations now available. The ones that have been more effective in my hands for anal and anogenital pruritus are two which are not on the market now but should be soon. They are Florinef-S with Mycostatin Cream* and Florinef-S Cream.* Each of these preparations also contain neomycin and gramicidin. I have found these effective in 90% of the cases. If these hydrocortisone or fludrocortisone preparations are to be effective, they will give relief from itching immediately. Therefore, due to the expense of these drugs to the patient it is well to prescribe a small tube at first. For the 10% who do not respond to this preparation I find a response usually to Perazil Cream** or Prantal Cream† 2 per cent.

This can be said about the new corticosteroid preparations. They are a "near-specific" for anal and anogenital pruritus and their introduction has changed the whole picture of the treatment of pruritus ani. They have made all other forms of treatment obsolete. The radical surgery, as the Ball operation and its modifications which was, according to some of us, the most effective treatment in the past, is no longer indicated. Surgical treatment is still indicated and should be done before other treatment is instituted, but it is the surgery of associated disease such as hemorrhoids, fissures, fistulas and crypts. If the lesion associated with pruritus ani is not removed other treatment is only palliative.

The proctologist is particularly trained in the diagnosis of disease associated with pruritus ani, and with his surgical skill and the availability of newer and more effective corticosteroids, his role in the treatment of anal and anogenital pruritus is now much easier than it was in the past.

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*Supplied by Dr. Gavin Hildick-Smith of The Squibb Institute of Medical Research, New Brunswick, N. J.

**Burroughs Wellcome, Tuckahoe, N. Y.

†Schering Corporation, Bloomfield, N. J.

Virus Studies in Acute Aseptic Meningitis and Poliomyelitis in Louisville: 1956-1958

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Accumulating knowledge concerning the enteroviruses will no doubt lead to a complete reclassification of the viral diseases affecting the central nervous system, including poliomyelitis.

ONE HUNDRED AND TWENTY-FOUR CASES of aseptic meningitis (including 32 with paralysis) were studied in the Children's Hospital and in the Louisville General Hospital from 1956 to 1958. These were chiefly sporadic cases, unlike the situation of epidemic paralytic poliomyelitis which occurred in 1950, 1952 and 1954. This report is to discuss the aims, methods and results of the investigation, and to discuss, in general, the enteroviruses.

The Enteroviruses

Current thinking has grouped polioviruses, Coxsackie viruses and ECHO viruses under the heading of enteroviruses because of certain common characteristics.[1] Enteroviruses are found in the human enteric tract, may invade the bloodstream and the central nervous system as well as other organs. Epidemiologic characteristics of each of the three groups further substantiates their being grouped together. Although distinct clinical syndromes may be produced by each of the groups there is considerable overlapping of the disease entities caused by each group. In addition, each of the groups may produce clinical spectra that vary from subclinical to fatal infection.

In table 1 the clinical entities associated with each group of the enteroviruses is presented. Perhaps the similarities of the diseases produced by each of the groups is deserving of more emphasis than the dissimilarities. Evidence for the paralytogenic activity of nonpolio viruses has been accruing and has recently been summarized by Steigman.[2] The ability of the Coxsackie and ECHO viruses to produce clinical paralytic poliomyelitis is of more than academic interest, if for no other reason than to appraise accurately the neurotropic potential of these viruses in the medical care of cases and their contacts, and to explain some of the paralytic disease occurring in children adequately vaccinated against poliovirus. Realizing that the syndromes of aseptic meningitis produced by each of the groups are clinically indistinguishable is helpful in fostering a conservative attitude with regard to early prognosis and convalescent immune status. An erroneous diagnosis of nonparalytic "poliomyelitis" may have the unfortunate effect of creating a false sense of security with regard to not needing routine poliomyelitis vaccination. While the nonspecific febrile illnesses produced by each of the groups are etiologically impossible to diagnose in individual cases on clinical grounds, awareness of the spectrum of disease states produced by these viruses may be of diagnostic value if case contacts are investigated.

The reasons for grouping the Coxsackie viruses and the ECHO viruses together under their respective headings are based on common biologic properties found in each group. The ability of the Coxsackie viruses to produce disease in suckling but not adult mice distinguishes this group. The types of lesions produced in the suckling mice enable the subdivision of the Coxsackie viruses into two groups, A and B. Each of the Coxsackie viruses produces specific serum neutralizing antibod-

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TABLE 1

ENTEROVIRUSES

	VIRUS DISEASE	
Polioviruses	*Coxsackie viruses*	*ECHO viruses*
Types 1, 2 and 3	Group A (Types 1-20) Group B (Types 1-5)	Types 1-19
Poliomyelitis 1. Paralytic 2. Nonparalytic ("aseptic meningitis") 3. Abortive	Acute aseptic meningitis (A and B) Herpangina (A) Bornholm disease (epidemic pleurodynia) (B) Meningoencephalitis (A and B)	Acute aseptic meningitis Febrile exanthems Gastroenteritis Paralytic poliomyelitis
Meningoencephalomyelitis Myocarditis Nonspecific febrile illness Subclinical infection	Benign pericarditis and "idiopathic" myocarditis (A and B) Paralytic poliomyelitis (A and B) Nonspecific febrile illness Subclinical infection	Nonspecific febrile illness Subclinical infection

ies in susceptible hosts; however, the serologic relationship of each virus to others in the group is not clearcut and, although there are some serologic cross reaction and heterotypic responses produced by the viruses, it is not really on a serologic basis that the Coxsackie group is established, but rather upon the property of pathogenicity in the suckling mouse.

The ECHO (Enteric Cytopathogenic Human Orphan) viruses are grouped together because they are found in human intestinal tracts, because they are cytopathogenic in primate tissue culture and because they are not pathogenic for suckling mice. There is not, as far as is known, a common antigen for the entire group. However, there are some of the group which do have common antigens.

Studies in Louisville Cases

In the Louisville study, clinical, epidemiologic and laboratory phases of each case were investigated. Of the 124 cases seen, 92 were diagnosed clinically as "aseptic meningitis"

TABLE 2

MONTHLY DISTRIBUTION OF 124 CASES OF ASEPTIC MENINGITIS AND POLIOMYELITIS ACCORDING TO LABORATORY DIAGNOSIS

1956	*Poliovirus Type 1 Paralytic Case*	*Poliovirus Type 1 Nonparalytic Case*	*Coxsackie*	*ECHO*	*CP Agent, Nonpolio*	*Negative*	*Totals*
June	0	0	0	0	0	0	0
July	0	1	5	1	0	9	16
Aug.	2	2	9	1	2	7	23
Sept.	3	2	3	4	0	4	16
Oct.	1	0	2	0	0	1	4
Nov.	2	0	0	0	0	1	3
Dec.	3	0	0	0	0	3	6
1957							
Jan.	1	0	0	0	0	2	3
Feb.	0	0	0	0	0	0	0
Mar.	1	0	0	0	0	0	1
Apr.	0	0	0	0	0	0	0
May	0	0	0	0	0	0	0
June	1	0	0	1	0	2	4
July	5	0	3	1	0	7	16
Aug.	6	1	2	3	0	5	17
Sept.	5	0	2	0	2	2	11
Oct.	1	1	0	0	0	1	3
Nov.	1	0	0	0	0	0	1
Dec.	0	0	0	0	0	0	0
1958							
Jan.	0	0	0	0	0	0	0
Feb.	0	0	0	0	0	0	0
Mar.	0	0	0	0	0	0	0
Totals	32	7	26	11	4	44	124

TABLE 3

ASEPTIC MENINGITIS STUDY (72 Cases)
June 15, 1956 through May 31, 1957

*Total Examined in MKTC**		*Polio*	*Coxsackie*					*Presumptive ECHO***	*CANP†*	*Negative*	*Total Isolated*
			B1	*B2*	*B3*	*B4*	*B5*				
Stool	67	18	1	3	1	8	1	6	1	28	39
C.S.F.	33	0	0	0	0	0	1	0	1	31‡	2

Negative MKTC Specimens in Suckling Mice

	Positive	*Negative*	*Incomplete*
Stool	5	23	2
C.S.F.	1	12	9

*MKTC—Monkey kidney tissue culture.
**Cytopathogenic in MKTC, nonpathogenic in suckling mice, not yet serotyped.
†Cytopathogenic in MKTC, nonpoliovirus, unidentified.
‡Includes 9 specimens obtained from patients whose stools yielded poliovirus.

and 32 were called paralytic poliomyelitis. Etiologic diagnoses were not possible on clinical grounds in the nonepidemic situation. The cases were sporadic with peak incidences in summer and early fall of each year (Table 2). Epidemiologic investigation revealed no apparent correlations among the index cases. Laboratory studies were concerned with attempts at viral isolations in monkey kidney tissue culture and/or in suckling mice (less than 24 hours old) from stool specimens and the cerebrospinal fluid. Specimens that were noncytopathogenic in monkey kidney tissue culture were injected into suckling mice by the intracerebral and/or subcutaneous routes. The patients' serum titers against the three serotypes of poliovirus were determined. Serotyping of the isolates was, for the most part, done by Dr. Kalter at the Communicable Disease Center, Chamblee, Georgia.

A total of 118 stools was examined in monkey kidney tissue culture (Tables 3 and 4). Thirty-nine were shown to have poliovirus (all Type 1); 20 contained Coxsackie virus; 11 contained ECHO virus; 3 contained nonpolio cytopathogenic agents (still unidentified); and 45 were negative.

Thirty-nine of the stools negative in tissue culture were injected into suckling mice; 4 isolates were thus obtained, only one of which has been serologically typed (Coxsackie A 7). The other three have not yet been typed.

A total of 75 cerebrospinal fluid (C.S.F.) specimens was examined in monkey kidney tissue culture: 24 of these specimens, obtained from patients whose stools yielded poliovirus, were negative; of the remaining 51 C.S.F. specimens one yielded Coxsackie B 5 and 2 others nonpolio cytopathogenic agents. (Coxsackie isolates were obtained from the stools corresponding with these last two); 48 others were negative.

Of these 48 specimens, 19 were injected into suckling mice; an untyped agent was isolated

TABLE 4

ASEPTIC MENINGITIS STUDY (52 Cases)
June 1, 1957 through March 15, 1958

*Total Examined in MKTC**		*Polio*	*Presumptive Coxsackie***	*Presumptive ECHO****	*CANP†*	*Negative*	*Total Isolated*
Stool	51	21	6	5	2	17	34
C.S.F.	42	0	0	0	1	41‡	1

Negative MKTC Specimens in Suckling Mice

	Positive	*Negative*	*Incomplete*
Stool	1	12	4
C.S.F.	0	6	20

*MKTC—Monkey kidney tissue culture.
**Cytopathogenic in MKTC, pathogenic for suckling mice, not tested in adult mice, not yet serotyped.
***Cytopathogenic in MKTC, nonpathogenic in suckling mice, not yet serotyped.
†Cytopathogenic in MKTC, nonpoliovirus, unidentified.
‡Includes 15 specimens obtained from patients whose stools yielded poliovirus.

from one specimen; the remaining 18 were negative.

An interesting case among the group studied was that of a 3 year old white boy who presented clinically as paralytic poliomyelitis. Serial muscle analyses were done until one year after the onset of his disease and revealed residual asymmetric pareses of muscle groups of his lower extremities. A stool specimen at the time of onset was noncytopathogenic in monkey tissue culture but was pathogenic in suckling mice; the agent was identified as Coxsackie A 7. Paired sera as well as a late convalescent serum revealed no demonstrable antibodies to the three serotypes of poliovirus; acute and convalescent sera showed a rise in titer of antibodies to Coxsackie A 7 from 1:6 to 1:630. The child had received no Salk vaccine. We believe his paralytic poliomyelitis was actually caused by the Coxsackie A 7 strain of virus recovered from him.[3]

Discussion

This representative group of 125 cases of viral infection of the central nervous system seen in a nonepidemic period brings out the importance of an etiologic diagnosis. Practical diagnostic technics have only recently been developed and the facilities for performing such studies are very limited. In special instances and for research purposes some such studies are done in the Kentucky Child Health Foundation Laboratory of the University of Louisville; the Laboratory of the State Board of Health has facilities for performing these tests and for forwarding appropriate specimens to the Communicable Disease Center Laboratory at Atlanta, Georgia.

Although poliovirus has commanded the greatest amount of attention in the field of nonencephalitic viral infections of the central nervous system, it is apparent that an array of viruses needs to be considered in a correct appraisal of the problem. With an increasing number of children successfully vaccinated with Salk poliomyelitis vaccine, it will be all the more important to make possible an etiologic diagnosis in patients with viral infections of the central nervous system for such different reasons as: (a) not impugning the efficacy of the vaccine in cases of aseptic meningitis and paralytic disease where nonpolioviruses are etiologically responsible; (b) gathering a better understanding of the ecology of these different viruses; and (c) for medical, legal and record purposes, such as concern special insurance policies, etc.

Classifications and comments made today in this rapidly moving field may be soon outmoded; it is evident that continued investigations must be made if the picture is to become clarified.

Summary

1. A general discussion of the enteroviruses, their biologic properties and clinical potential, has been presented.

2. Results of a clinical, epidemiologic and laboratory study of 124 cases of aseptic meningitis and paralytic poliomyelitis have been presented.

3. A case of paralytic disease caused by Coxsackie A 7 virus has been mentioned.

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Evaluation of Some New Anthelminthic, Anticholinergic, Hydrocholeretic, and Antispasmodic Drugs*

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New drugs for use in the field of gastroenterology continue to be produced by the pharmaceutical industry. The average doctor finds difficulty in evaluating the claims made for these new products. Studies such as the ones reported here are helpful to the practitioner.

EVALUATION OF THE THERAPEUTIC EFFICIENCY of agents used in clinical gastroenterology is extremely difficult, even when a most exacting program is followed and every effort is made to avoid misinterpretation. Laboratory and radiologic studies do not permit accurate determination of therapeutic achievement in all dysfunctions and diseases. Moreover, controls are not applicable to all studies; double-blind studies and placebo controls have yielded confusing results.

The present report concerns an attempt to establish the value of a group of therapeutic agents in certain gastrointestinal disturbances. One specific agent, an anthelminthic, has definite, measurable effects, requires no control, and is not affected by bias or patient-physician relations. The effect of the hydrocholeretic agents depends on the control period, and whereas it is not influenced by the physician's rapport, it cannot be measured sufficiently accurately by presently available methods. The agents used in peptic ulcer cannot be adequately controlled, must be employed cautiously in subjects susceptible to psychic influence, and are difficult to evaluate objectively because of the variability of control subjects, patients, the disease, and the response. The intestinal normalizer can be adequately controlled and measured, and its evaluation is less subject to bias or the physician's personal equation. The tranquilizers, on the other hand, defy evaluation by any method, including double-blind studies.

Intestinal Parasites

That an effective agent against all pathogenic intestinal parasites may soon be commercially available holds reasonable promise. Ethyanine, (3, 3'-Diethylthiadicarbocyanine iodide), a cyanine dye with minimal toxicity, has eradicated intestinal nematodes in animal experimentation.[1-3] The clinical observations of Swartzwelder,[4] Malice,[5] Hoekenga,[6] and Frye[7] have confirmed its effectiveness against *Ascaris lumbricoides, Trichuris trichiura, Enterobius vermicularis* and *Strongyloides stercoralis*. Whereas its efficacy against *Necator americanus* has also been suggested in animal studies,[3] this has not been unequivocally con-

*Panel Discussion on Therapeutic Advances in Gastroenterology, Section on Gastroenterology, Southern Medical Association, Fifty-First Annual Meeting, Miami Beach, Fla., November 11-14, 1957.

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The drugs used in these studies were obtained from the following sources: Ethyanine was supplied by Dr. J. B. Hammond of the Eli Lilly Laboratory for Clinical Research, Indianapolis; Tral by Dr. George Berryman, Scientific Division, Abbott Laboratories, Chicago; Pathilon chloride, Pathilon iodide, and Pathibamate by Dr. Jack McConnell of Lederle Laboratories, Pearl River, N. Y.; Zanchol by Dr. William Crosson of the Research Division of G. D. Searle and Co., Chicago; Benulose by the Medical Research Department of The Wm. S. Merrell Co., Cincinnati; Pro-banthine with Dartal by Dr. Thomas Hayes of G. D. Searle Company, Chicago; Prantal with Trilafon by Dr. G. Kenneth Hawkins of Schering Corporation, Bloomfield, N. J.; Nostyn by Dr. Norman Heminway of Ames Co., Elkhart, Ind.; and Marsilid by Dr. Steven Sawchuk of Hoffman-La Roche, Inc., Nutley, N. J.

firmed in human patients.[4,5] Ineffectiveness against *Hymenolepis nana* and *Entamoeba histolytica* has been recorded.[7] As a result of these studies, the recommended dosage for adults is 600 mg. daily for 5 days or, if necessary, as long as 10 days or more. Gastroenteric side effects, such as nausea, vomiting, diarrhea, colic, and bloody stools, although evanescent, have resulted in production of enteric-coated tablets.

Ten normal persons were used as control subjects to evaluate tolerance and toxicity of Ethyanine. The recommended dosage schedule of 600 mg. daily (in 3 equal doses of 100 mg. enteric-coated tablets) for 5 days was used. No change was observed in renal, hepatic, or hematologic phenomena at the end of treatment or 30 days thereafter. Six patients had side effects: 3 had nausea; one had nausea, vomiting and abdominal cramping. All manifestations were transient and, except in the patient with vomiting, were mild; discontinuance of medication promptly effected their subsidence. Seven persons who refused to complete the therapeutic course are not included in this study.

During the 5 months of the study, 45 patients have been under management for a total of 57 parasitizations; 5 of these patients had 3 parasites and 2 had 2 parasites. *Chilomastix mesnili, Trichomonas hominis* and *Entamoeba coli,* all considered nonpathogenic, accounted for 12 of those parasites found in combination. Remarkably favorable results were obtained against the pathogen *Strongyloides stercoralis* and the possible pathogen *Trichuris trichiura,* against which previously employed preparations have been distressingly ineffective (Table 1). Enthusiasm for its effectiveness against *Enterobius vermicularis* is reserved by the fact that the piperazines have been equally effective without as significant side effects. Because we had only 2 patients with ascariasis in the series, no conclusion is justified about the value of this drug in its treatment. Ineffectiveness of Ethyanine against *Entamoeba histolytica, Necator americanus, Giardi lamblia,* and *Entamoeba coli* has been substantiated by our studies.

In these 45 patients no renal, hematologic or hepatic abnormality occurred during or after treatment. Side effects were observed in 14 patients: nausea in all, emesis in 3, abdominal pain in 6, and diarrhea in four. All symptoms were transient, being limited to the duration of medication. Two patients refused to continue treatment because of severity of abdominal pain and vomiting.

The search for a more satisfactory and complete amebicide has continued despite a progressive decline in the incidence of amebiasis. We have recently had under evaluation Amebicida Doryan. Although preliminary results have been excellent, our studies are still too limited to permit any conclusion at this time except that more intensive evaluation seems warranted.

Peptic Ulcer

According to Illingworth,[8] "All established methods of medical treatment are based on two main principles, to control or neutralize

TABLE 1
PARASITICIDAL EFFICACY OF ETHYANINE
(600 mg. Daily for 5 Days)

Parasite	Number of Infections	Therapeutic Effect of Ethyanine			Average Duration Follow-Up (Days)
		Eradication	Improvements*	Failure	
S. stercoralis	14	9	2	3**	42
E. vermicularis	9	7	0	2	49
T. trichiura	6	4	1	1	29
T. hominis	6	4	0	2**	28
E. histolytica	6	0	0	6	
G. lamblia	5	0	0	5	
E. coli	4	0	0	4	
N. americanus	3	0	0	3	
A. lumbricoides	2	2	0	0	28
C. mesnili	2	2	0	0	28
Total	57	28	3	26	

*Reduction in egg count
**Discontinued because of side effect

acid juice and to put the diseased part at rest." With this concept in mind, we have recently evaluated two newer and more satisfactory combined gastric secretory and motility inhibitors, which we hope will serve "to put the diseased part at rest." The first of these two, Hexocyclium (Tral), has the additive feature of sustained action. The second, Pathilon chloride, promises to have all the advantages of Pathilon iodide but to be free of the objectionable interference with iodine uptake studies.

Hexocyclium. Tral, one of the newer quarternary ammonium salts, N-(β-cyclohexyl-β-hydroxy-β-phenylethyl)-N'-methylpiperazine methosulfate, is a potent postganglionic blocking agent.[9-11] In our studies, the effective dosage varied from 25 to 75 mg. 4 times daily (before meals and on retiring). Single doses of 50 to 75 mg. exerted satisfactory influence on gastric secretion and motility, with only moderate xerostomic side effects. Controlled observations (beyond 6 months) in 52 patients have failed to yield evidence of tolerance, and only moderate anticholinergic side effects have been noted. Film-sealing of the tablets obviated the unpleasant bitter taste. Of 25 patients with duodenal ulcer, under continuous therapeutic evaluation for 24 months or more, symptoms disappeared completely in fifteen. Mild, persistent, but nonspecific, digestive complaints replaced manifestations of true ulcer in 7 patients who, nevertheless, considered the agent definitely beneficial. Ulcers became reactivated in the other 3 patients during treatment; complicating hemorrhage in one required resection, and the other 2 abandoned Tral for other agents. Complete healing without deformity was evident on radiologic examination in 8 patients, residual duodenal deformity without demonstrable ulcer crater in 7, persistent but smaller ulcer in 4, no change in 3, and worsening in the remaining three.

For more satisfactory, sustained anticholinergic action, Hexocyclium has been embedded, at various bores and depths, in a plastic matrix, from which the drug can be leached when exposed to the dissolving effect of gastrointestinal fluids. The underlying concept is that this new preparation is independent of gastric acidity or other factors involved in release of drugs from ordinary enteric coating. Thus, the disadvantages of variable release are theoretically avoided, since a steady leaching effect is achieved, with smooth onset and decline. Among 25 patients to whom 75 mg. of sustained-action Tral was administered at night, secretion was completely inhibited within one to ten hours in 14; suppression of hydrochloric acid exceeded 50% of that observed in the control subjects in 6 and was less than 20% in the other five. On study of gastric motility, with the use of barium, 10 hours after administration of the drug, ineffective gastric peristalsis and duodenal atonicity were noted. Eighteen of the 25 patients complained of mild xerostomia and visual blurring for 10 hours after administration of the drug; one had mild facial flushing and vertigo. Neither dysuria nor constipation was observed.

After preliminary clinical evaluation of tolerance, the preparation with sustained-action was substituted; equivalent doses were administered but only twice a day, one in the morning and one at bedtime. Selected for this control study were 20 patients with duodenal ulcer in whom regular Tral had favorably influenced gastric secretion as well as clinical symptoms, with only moderate xerostomic effects. Ten patients had received 100 mg. daily and the other 10 had received 200 mg. daily. The drug with sustained-action still produced xerostomia and visual blurring, but these effects were estimated to be less discomforting in all except 2 persons. No evidence of a cumulative effect or sudden release was observed. Symptomatic response was complete in 7, and improvement was recognized by an additional 2, of the persons who received 100 mg. daily, whereas symptoms disappeared in 5, and improvement was evident in all, who received 200 mg. daily. Pain was refractory in only one patient who received 100 mg. daily; when he later underwent operation, he was found to have associated pancreatic involvement consequent to perforation of the ulcer. In all remaining patients who obtained a satisfactory response beyond 3 months, a single maintenance dose of one-half the original amount, administered at night, proved to be satisfactory. At the end of 6 months, healing of the ulcer crater, with residual deformity, was demonstrable on roentgenographic examination of 6 patients who received 100 mg. and of 7 who received 200 mg. of the drug. Improvement, but with a persistent smaller

crater, was observed in the remainder. When compared with regular Tral, this preparation was found to be equally effective, with minimal side effects and greater ease of administration.

Pathilon chloride. A 25 mg. tablet of Pathilon chloride contains 22.3 mg. of the Pathilon base, as contrasted with 17.9 mg. in a tablet of Pathilon iodide. This preparation was tested for two possible advantages: absence of the disadvantages of iodide content and possible greater potency. In comparable studies in a series of 15 patients, no measurable differences in effect on gastric secretion and motility have been noted. When Pathilon chloride was substituted for Pathilon iodide in 25 patients, no difference in side effects was observed; 12 patients experienced moderate xerostomia and visual blurring. Detailed laboratory evaluation failed to yield any evidence of hematologic, renal, or hepatic abnormality during a period of observation exceeding 30 days. On the basis of such short-term clinical evaluation, symptomatic response has appeared to be as satisfactory with the chloride as with the iodide preparation, but no definite conclusion regarding therapeutic efficiency is justified at this time. Further clinical evaluation of two promising new anticholinergic agents is to be encouraged for better understanding of that portion of the problem of ulcer related to vagally stimulated gastric hypersecretion and hypermotility.

Biliary Dysfunction and Disease

Zanchol. Successful hydrocholeresis is essential for better management of disease of the biliary tract. The most recent drug introduced to combat this disease is Zanchol, a brand of florantyrone. This synthetic drug [Y-oxo-Y-(8 fluoranthene) butyric acid], which proved to be innocuous in laboratory study, produced more sustained and profuse hydrocholeresis than dehydrocholic acid, with less secretion of biliary solids when given in therapeutic dosage.[12] According to McGowan,[13,14] florantyrone induced favorable alteration in biliary flow, color, viscosity, sedimentation and bacterial content, with detergent effect and action on parenchymal hepatic cells. He observed no untoward reactions. In another study, in which 7 patients with chronic hepatic disease were treated for 84 days, side effects included increased abnormality in hepatic function, transient eosinophilia, and weight loss.[15]

In a series of 58 of our patients with symptoms of biliary dysfunction who were given 4 to 6 tablets of 250 mg. each of Zanchol for periods up to 28 days, mild anticipated abdominal cramping and diarrhea could not be interpreted as side effects but were rather considered an index of therapeutic activity. No hematologic, renal, or hepatic abnormality could be attributed to the drug during this period. Weight loss was not common in our patients. In 12 patients who received Zanchol for 4 to 6 days during convalescence from cholecystectomy and choledochostomy, biliary flow was appreciably increased within 24 hours (average 120 cc.). Alteration in viscosity was hardly measurable, although the bile appeared thinner and clearer and changed from amber to a clear green hue. Grass sediment progressively diminished, and shaking always resulted in increased accumulation of foam. Withdrawal of the drug caused the bile to revert to its pretreatment characteristics within an average time of 14 hours. Transducer studies demonstrated no alteration in intracholedochal pressure.* Nor could we confirm other evidence of detergency or influence on bacterial flora.

Twenty-five patients with clinically diagnosed, chronic, noncalculous cholecystitis (normal hepatic function with functional cholecystographic abnormality) were treated with Zanchol for 4 months. Ten obtained concomitant symptomatic and cholecystographic improvement, 13 obtained symptomatic response but demonstrated no change on cholecystographic examination, and a single patient failed to show symptomatic or cholecystographic amelioration. Symptomatic response has continued in 15 patients despite discontinuance of the drug. Recurrent dyspeptic symptoms in 10 patients disappeared upon restitution of therapy.

Fifteen patients with abnormal cholecystograms and calculi were given Zanchol for 10 days preoperatively. Nine obtained symptomatic improvement, 5 had persistent dyspepsia, only one patient experienced a bout of biliary colic.

Six patients in the study had previously

*Intraluminary choledochal studies were performed by Dr. John Leckert of the Department of Cardiology, Browne-McHardy Clinic, New Orleans, La.

undergone cholecystectomy and were to be operated on again for obstructive jaundice; 2 were to undergo operation for choledocholithiasis, 2 for stricture of the common duct, and 2 for remnant of the cystic duct. After administration of Zanchol, an increase in choledochal drainage of these patients was observed (average 140 cc. per 24 hours).

In a few patients administration of Decholin during a control period stimulated profuse hydrocholeresis but did not produce the change in color or sediment associated with Zanchol. We do not consider the diminished excretion of biliary solids advantageous. If biliary stasis is actually an etiologic or contributing factor in disease of the biliary tract, hydrocholeretics, such as florantyrone, would appear, from our experience, to be specifically indicated.

Intestinal Normalization

Abnormal defecation, as a result of intestinal abuse from laxatives and enemas, functional spasticity or atonicity, or secondary to nonobstructive inflammatory changes or a healing process, can be corrected in the cooperative patient. Careful clinical direction and use of such adjunctive agents as hydrophilic colloids or wetting agents, alone or in combination with antispasmodics or laxatives, can achieve this purpose. Benulose, a modified, more osmotic sodium carboxymethyl-cellulose, used in conjunction with sodium lauryl sulfate and an antispasmodic, Bentyl hydrochloride, proved to be effective in 162 or 90.1% of 179 of our patients with functional intestinal derangements and in 58 or 80.5% of 72 patients with inflammatory disturbances.[16] Neither side effects, habituation, nor tolerance to the drug developed.

Antispasmodic Agents

It has been estimated that during the year 1956, 30,890,000 prescriptions were filled for antispasmodics, including both natural and synthetic compounds.[17] The retail cost of these prescriptions totaled approximately $75,446,000.00. Obviously, this great demand for antispasmodics stimulates continued trial and production of new agents, as well as modification of available agents to provide sustained or tranquilizing action.

Tranquilizers. Abnormal esophageal tonicity cannot be managed practically by any so-called antispasmodic. Its innervation is such that vagal blocking agents enhance manifestations related to achalasia. Motility of the stomach and upper intestinal tract are definitely inhibited by the newer atropine-like drugs. In our experience, tranquilizers have not enhanced this action; any additive influence must be accredited to the sedative action that alleviates emotional manifestations. We have used Pathibamate, Pro-banthine with Dartal, and Prantal with Trilafon. In a series of patients with gastrointestinal disease presumably related to the psyche, tranquilizers have proved of some assistance in management of certain entities and of no value in other diseases. In control studies in 50 patients with duodenal ulcer, Dartal, Nostyn, Pathibamate, and Trifalon have been equally effective for control of nausea, vomiting, and tension associated with active phases of the disease. We believe that small doses, half the amount advocated by the manufacturer, are best to avoid depressing side effects. A small series of 9 patients with duodenal ulcer have recently been under dietary management, with a tranquilizer (Nostyn) as the only supplemental medication. Although it is still too early to draw any definite conclusions, all 9 have remained asymptomatic. Nostyn has not been associated with any side effects and is milder and more delayed in action than any of the other agents. Meprobamate, although rapid in action, has produced occasional side effects of dermatitis, excitation, mild depression, and withdrawal anxiety in our patients. Dartal and Trilafon have caused mild fatigue and weakness in the legs but have otherwise been entirely satisfactory.

In a small series of 12 patients with chronic ulcerative colitis, these same agents appeared to have increased the mixed anxiety and depression that plague these patients. A component that produces true despondency has been attributed to these drugs in 7 of our patients who experienced progressive deteriorative emotional changes, and accentuation of manifestations related to chronic ulcerative colitis necessitated their discontinuance. In 4 of these 7, substitution of Marsilid, in dosage of 150 mg. daily, resulted in a degree of euphoria, stimulation of appetite with consequent gain in weight, and symptomatic improvement.

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EDITORIALS

THE MUSCLE BIOPSY

The use of this means of diagnosis in suspected systemic disease comes up frequently for consideration. All too often the clinician or house-officer expects too much from it, qualitatively speaking. The experienced physician has been disappointed so often, if not surprised, by a negative result in quite obvious systemic disease that he recognizes the possibility of an unrewarding procedure. These facts often deter him from asking for a biopsy in a hospitalized private patient for whom an operating-room fee, surgeon's fee and a couple of additional days in the hospital may easily add up to a hundred dollars more or less. The possibilities of a positive diagnosis must be balanced against this fact.

A recent review by a group[1] from the Columbia-Presbyterian Medical Center, of New York, is of interest in regard to the results of muscle biopsy. Over an 11 year period (1946-1956), 552 muscle biopsies were done in 519 patients, 102 of which were done in 89 patients having neurologic disease and thus outside of the categories which stimulated interest for this review.

The study was for the purpose of evaluating the muscle biopsy in the diagnosis of trichinosis, sarcoidosis, polyarteritis, disseminated lupus erythematosus and dermatomyositis (including polymositis). The diagnoses in the cases reviewed were established on clinical grounds, with the assistance of tests accepted as specific, and by diagnosis from tissue changes,—biopsy or autopsy.

The great majority of biopsies came from the gastrocnemius muscle, because of its accessibility, though a goodly number were from the deltoid muscle also. Three levels in the biopsy block were cut routinely. It is pointed out that in a muscle biopsy changes may be found in the muscle fiber itself, in the interstitial connective tissue and in the blood vessels.

The vascular changes may vary in degree from an inflammatory infiltration of round cells about arteries or arterioles and arteritis without necrosis, to acute arteritis with varying degrees of necrosis in the arterial wall and with or without inflammatory granulomas related to the arteries. (Perivascular inflammatory reaction may also be found related to veins or venules.)

The changes encountered in the interstitial connective tissue were in the main inflammatory, particularly with a lymphocytic reaction. Whether this inflammatory reaction is diffuse, focal or perivascular seems of secondary importance from a diagnostic standpoint, since any of these three distributions may be found in the several clinical entities related to the rheumatoid state and thus is not of specific importance. In instances of sarcoidosis the typical granuloma was found in the interstitial tissue, consisting of epithelioid cells commonly with giant cells.

The pathologic changes in the muscle fibers may vary greatly from minimal degenerative changes, which may need to be discarded as of no diagnostic significance, to clear-cut degeneration and replacement by fibrosis. The vascular change and/or inflammatory reaction in the interstitial tissue usually accompanied the greater degrees of degeneration in the muscle fibers to aid in a definitive pathologic diagnosis. The diagnostic finding of trichina larvae in muscle fibers appeared only in 3 of 15 cases; others showed mere perivascular inflammation. In 22 of 42 instances of sarcoidosis the diagnostic granulomas were found. In another 25 patients in whom sarcoidosis was not diagnosed clinically, but in whom the disease could not be ruled out, no sarcoid granulomas were found. In cases of polyarteritis, even though the vascular lesions were characteristic, changes in the muscle fibers appeared in less than half. Degenerative changes in muscle fibers were occasionally encountered in muscle biopsies from instances of disseminated lupus and rheumatoid arthritis. Though very frequent and of greater severity in cases of dermatomyositis and polymyositis, the authors pointed out that such findings appear so frequently in other conditions that they have no clear-cut diagnostic specificity.

1. Wallace, Stanley L., Lattes, Raffaele, and Ragan, Charles: Diagnostic Significance of the Muscle Biopsy, Am. J. Med. 25:600, 1958.

In summary, the authors point out that the muscle biopsy may be of relatively little help in clinical diagnosis, and from their review found specific diagnostic changes only in some patients having trichinosis, sarcoidosis and polyarteritis,—20%, 50% and 37% respectively. They refer to discussions in the literature of the vascular, inflammatory and degenerative changes found in interstitial and muscle tissue in diseases of the "rheumatoid state,"—disseminated lupus, rheumatoid arthritis, rheumatic fever scleroderma, and serum sickness. They dismiss these by recounting the findings of the several lesions which have been described and their incidence in a variety of conditions unrelated to possible tissue sensitivity.

If one chooses from the authors' tables those cases just referred to, one finds they have in their material 113. One finds further that 25% of these showed "perivascular or diffuse inflammation," 30%, "muscle degeneration," 6 instances of "muscle atrophy," and one of arteritis with, and one without necrosis. Of the 113, only 20% revealed no abnormal findings. It must again be emphasized that the authors chose not to discuss these other than to say, and properly so, that they are not of diagnostic specificity.

Wallace and his co-workers have presented the cold scientific facts which put the muscle biopsy in its proper perspective. Nevertheless, the finding of certain changes, though not diagnostically specific, often add most helpful aid in a puzzling clinical situation, and in a diagnosis ultimately proven to be correct. The muscle biopsy, like the electrocardiogram, the cholecystogram, L.E. cell and, in fact, most laboratory procedures, may not be specifically diagnostic but, when fitted properly to a good history and physical examination, may offer another piece in the jig-saw puzzle of a difficult diagnosis. The expense of getting a muscle biopsy as against the possibility of a specific diagnosis or as an aid in diagnosis makes its choice more of a niceity than for most other laboratory procedures.

25 YEARS AGO

A Comparative Study of the Value of Tetrachlorethylene As a Means of Ultimate Control and Eradication of Hookworm Disease in Children*

"Having attended practically every meeting of the Southern Medical Association since its organization, I am well aware of the fact that the subject of hookworm disease has occupied a place on almost every program. In 1930, the laboratories of nine state departments of health in the South examined 121,388 specimens for hookworm infestation and found 34,134, or 22.1 per cent, positive for hookworm infestations. . . .

"Routine stool examinations were made on over 5,000 patients entering the Mississippi Baptist Hospital at Jackson, Mississippi. These were mainly adults who entered the hospital for surgical treatment. However, they revealed over 15 per cent infested with hookworm. Under the direction of the Mississippi State Department of Health, stool examinations were made in two of the United States Government Civilian Conservation Corps Camps located in south Mississippi, which revealed hookworm infestation in 199 out of 398, or 50 per cent. These young men came from 21 different counties in Mississippi.

"There have been only a few reports of the use of tetrachlorethylene in the treatment of hookworm disease in the South. . . .

"In 1928, after I had been selected physician to over 600 children in institutions located in the City of Jackson, a very careful health survey of the institutions was made with a thorough physical examination, including a stool examination, of each child. This revealed that over 51 per cent of these children were infested with hookworm. . . . It will be noted that these institutions were provided with city sewerage and all other sanitary advantages. The problem of soil pollution and reinfestations, which are always factors to be considered under field conditions, are entirely eliminated in this study.

"The oil of chenopodium proved ineffective in 39 per cent of the cases treated, which was revealed by frequent stool examinations, the last of which was made just before the next treatment was begun. . . .

"A complete resurvey of the entire number of children in the institutions was made just before the treatment with tetrachlorethylene was begun and there were found to be 218 with positive stools. . . . Of these 218 cases thus treated, stool examinations made four months after treatment revealed only 15, or approximately 7 per cent, remaining positive.

"The results obtained with tetrachlorethylene as compared with those of oil and chenopodium and carbon tetrachloride, by all who have had opportunity to make any comparison, even under field conditions, would indicate the absolute superiority of tetrachlorethylene."

*Garrison, Harvey F.: A Comparative Study of the Value of Tetrachlorethylene as a Means of Ultimate Control and Eradication of Hookworm Disease in Children, South. M. J. 27:24, 1934.

SOUTHERN MEDICAL NEWS

ALABAMA

Dr. J. Garber Galbraith, Birmingham, Councilor from Alabama for the Southern Medical Association, has been chosen President-Elect of the Jefferson County Medical Society. Dr. S. Joseph Campbell, Birmingham has succeeded Dr. W. E. Coleman as President, with Dr. S. Buford Word, Vice-President, and Dr. Wallace A. Clyde, Member of the Board of Health. In addition to officers, those elected to the Board of Trustees include: Drs. LeRoy Holt, H. N. Carmichael, Hal Ferguson, Joe Humphries, Hugh Linder, C. W. Neville, James K. Ward, S. Richardson Hill, G. J. Roscoe, William H. Kessler, Ed Harris, J. M. Burnett, Charles E. Porter, Arthur Freeman, E. Rhodes Johnston and Keehn W. Berry. Dr. Fay M. Randall was elected to the Grievance Committee for a one year term.

Dr. Robert W. Longley is a recent addition to the staff of the University of Alabama Medical Center, having joined the Department of Biochemistry as Assistant Professor. Dr. Longley was formerly of Dorn Laboratory for Medical Research where his work was entirely research.

The Second Medical Progress Assembly, sponsored by the Birmingham Academy of Medicine, will be held at the Tutwiler Hotel September 13-15, 1959, according to an announcement by Dr. Herbert H. Thomas, Chairman of the Publicity Committee.

Dr. Polly Ayers, Birmingham, Director of the Jefferson County Health Department Dental Service, is new President of the American Public Health Dentists.

The following physicians have been appointed as department chairmen for 1959 at East End Memorial Hospital in Birmingham: Dr. Wade Alford, Medical Department; Dr. J. Frank Trucks, General Practice; Dr. James W. O'Dell, Surgical; Dr. J. S. Jordan, Obstetrics-Gynecology, and Dr. P. A. Morgan, Radiology and Pathology.

Dr. D. L. Lovell is the new Director of the Medical Education and Intern Training Program at the Birmingham Baptist Hospitals.

Dr. William Klip, Utrecht, Holland, has recently joined the staff of the Alabama Medical Center as

Continued on page 50

BOOKS RECEIVED

Hospital Planning for the Anesthesiologist. By William H. L. Dornette, M.D., Professor of Anesthesiology and Head of the Department, The University of Tennessee College of Medicine, Memphis, Tennessee. American Lecture Series No. 335. 117 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $5.25.

Textbook of Microbiology. By Kenneth L. Burdon, Ph.D., Professor and Chairman, Department of Microbiology, Baylor University College of Medicine, Houston. Fourth Edition, 619 pages. New York: The MacMillan Company, 1958. Price $5.75.

Diagnostic Anatomy. By Weston D. Gardner, M.D., Associate Professor of Anatomy, Marquette University School of Medicine, Milwaukee, Wis. 360 pages. St. Louis: The C. V. Mosby Company, 1958. Price $10.00.

Human Blood in New York City. A Study of Its Procurement, Distribution and Utilization. 147 pages. New York Academy of Medicine, 1958.

War Blinded Veterans in a Postwar Setting. A Social Work Followup of Rehabilitation Measures for Blinded Veterans, Department of Medicine and Surgery of the Veterans Administration. 260 pages. Washington, D. C.: U. S. Government Printing Office, 1958. Price $1.50.

Expert Committee on Biological Standardization. Eleventh Report. World Health Organization Technical Report Series No. 147. New York: Columbia University Press, 1958. Price $.30.

Fibromyomas of the Uterus, edited by Robert A. Kimbrough, M.D., and *Toxemias of Pregnancy,* edited by Louis M. Hellman, M.D. Clinical Obstetrics & Gynecology. Volume 1, Number 2. 533 pages. New York: Paul B. Hoeber, Inc., 1958.

Therapeutic Uses of Adhesive Tape. Johnson & Johnson, New Brunswick, N. J., 1958. Free to doctors by writing the company.

Physical Diagnosis. By F. Dennette Adams, M.D., Physician, Board of Consultation, Massachusetts General Hospital. Fourteenth Edition, 879 pages. Baltimore: The Williams and Wilkins Company, 1958. Price $12.00.

Principles of Radiographic Exposure and Processing. By Arthur W. Fuchs. 276 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $10.50.

The Kidney. By H. E. de Wardener, M.B.E., M.D., F.R.C.P., Senior Lecturer in Medicine, St. Thomas's Hospital, London. 327 pages, 74 illustrations. Boston: Little, Brown and Company, 1958. Price $10.00.

The Waking Brain. By H. W. Magoun, Ph.D., Department of Anatomy, University of California School of Medicine. 135 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $4.75.

Homosexuality, Transvestism and Change of Sex. By Eugene de Savitsch, M.D. 120 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $3.50.

Bibliography of International Congresses of Medical Sciences. Prepared by W. J. Bishop for Council for International Organizations of Medical Sciences. 227 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $5.50.

Congenital Anomalies of the Hand and Their Surgical Treatment. By Arthur Joseph Barsky, M.D., Professor of Clinical Surgery, Albert Einstein College of Medicine, N. Y. C. American Lecture Series No. 311. 160 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $5.75.

Clinical Neuroanatomy, Neurophysiology and Neurology. By Louis Hausman, M.D., Professor of Clinical Medicine (Neurology), Cornell University Medical College and Clinical Professor of Neuropsychiatry, New York University College of Medicine. 478 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $9.75.

Human Dissection, Its Drama and Struggle. By A. M. Lassek, M.D., Department of Anatomy, Boston University School of Medicine. 285 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $6.50.

BOOK REVIEWS

Introduction to Biostatistics

By Huldah Bancroft, Ph.D., Professor of Biostatistics, Tulane University School of Medicine, New Orleans. 205 pages. New York: Paul B. Hoeber, Inc., 1957. Price $5.75.

This is a textbook presenting the material contained in the course the author has given in medical statistics for many years at Tulane. The presentation is kept simple and nontechnical. Simple presentations of subjects inherently not-so-simple sometimes say practically nothing useful, or else produce half-truths that may dangerously mislead the reader. The reviewer believes that this has not happened in this book; the author has produced a useful and readable text. The reviewer disagrees with the author on a number of small points of presentation, but on the whole the material is well handled. The book is inadequate to prepare its reader to handle unassisted all the statistical problems that can arise in even a simple research project, but it will enable him to more adequately assess the reports he reads in the literature, and aid him in reasoning objectively from his "sample" evidence as he treats individuals in his medical practice.

A welcome difference from the well-known text by Bradford Hill is that the numerous and in general excellent examples are more frequently real rather than hypothetical, with literature references cited. There is much more emphasis on clinical rather than public health problems. If read by the physician without benefit of an instructor, there would be some difficulties in profiting from the well-chosen problem sections, since no answers are given. The book is not so strong as Bradford Hill's on design of investigations (e.g., lack of adequate discussion of randomization), but slightly stronger on aspects of analysis (e.g., uses simple but adequate symbols for statistical measures; presents the t-test procedure). An excellent short discussion is presented of methods for estimating appropriate sample sizes before undertaking an investigation. This makes clear one of the reasons for the frequent lack of conclusiveness of reports in the literature,—study of insufficient numbers of subjects to give much chance of detecting any but very large true differences between groups.

Diagnostic Bacteriology

By Isabelle G. Schaub, A.B., Assistant Professor of Microbiology and Instructor in Medicine, The Johns Hopkins University School of Medicine; M. Kathleen Foley, M.A., Assistant Professor of Biological Sciences, College of Notre Dame of Maryland; Elvyn G. Scott, M.T., Bacteriologist-in-Charge, Department of Bacteriology, The Delaware Hospital; and W. Robert Bailey, Ph.D., Associate Professor of Biological Sciences, University of Delaware. Fifth Edition, 328 pages. St. Louis: The C. V. Mosby Company, 1958. Price $4.75.

This small book presents acceptable diagnostic methods for the medical bacteriology laboratory in clear and concise terms. It describes all the necessary procedures such as staining and examination of smears and cultures, preparation of media and stains, handling of specimens, as well as reading and interpreting results. On reading this manual one is impressed with its efficiency.

The fifth edition includes some new material not found in previous editions. This includes four new chapters and a new section on identification of pathogenic fungi as well as revision of numerous other sections in order to bring them up-to-date.

In addition to being a very useful manual for diagnostic laboratories, this book is a good reference for physicians who need to understand the details of tests in order to better evaluate their usefulness and limitations.

Uses of Epidemiology

By J. N. Morris, M.A., F.R.C.P., D.P.H. 131 pages. Baltimore: The Williams & Wilkins Company, 1957. Price $4.00.

This little book written by a top notch epidemiologist has a very refreshing and thought provoking point of view. One gets the impression that here is a man who considers himself, or probably more correctly epidemiology, to be at least the equal and probably superior to any of the clinical disciplines in ferreting out the causes of disease. However, he does point out that "Epidemiology is the only way of asking some questions in medicine, one way of asking others (and no way at all to ask many)." There are seven uses of epidemiology outlined by the author. They are:

1. Determining the history of the health of the community and of the rise and fall of diseases in the population. By looking at the past one may gain some insight into the future.

2. Measuring of the incidence, prevalence of morbidity and of mortality in a community would give one some idea of the changing health problems.

3. Appraising the needs and resources in the health services. These can be comparable between various populations.

4. Estimating or predicting the chances of an individual's acquiring a particular disease.

5. In helping to gain a more complete clinical picture by observing various forms of a disease and its character in other countries.

6. The identification of syndromes from the distribution of clinical phenomena among sections of the populations.

7. In searching for the causes of health and disease by employing the time-honored methods of epidemiology.

This is a book which all investigators should read and remember carefully because there is much of practical value. It should be required reading for medical students. It is perhaps too much to hope that the clinicians will read this book but there is much in

it that would be extremely helpful in the everyday practice of medicine.

Roentgen Diagnosis of Abdominal Tumors in Childhood

By Charles M. Nice, Jr., M.D., Alexander R. Margulis, M.D.; and Leo G. Rigler, M.D., all from the Department of Radiology, University of Minnesota Medical School. 70 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1957. Price $4.00.

This monograph is an excellent survey of roentgen signs and findings associated with and helpful in diagnosis of abdominal tumors found in childhood. Embryology and anatomy, as well as proper radiographic procedures, typical diagnostic findings and differential diagnoses are described. The conciseness and brevity without neglect of important information, are distinctive features and highly desirable. Illustrations are of excellent quality and illustrate the pathologic findings associated with the various lesions described.

The bibliography includes references of more detailed and statistical information dealing with the individual types of lesions.

The Student-Physician

Edited by Robert K. Merton, George G. Reader, M.D.; and Patricia L. Kendall. Introductory Studies in the Sociology of Medical Education. 351 pages. Cambridge, Mass.: Published for The Commonwealth Fund by Harvard University Press, 1957. Price $5.00.

This book is a collection of papers on continuing studies of the sociology of medical education begun several years ago by the Bureau of Applied Social Research at Columbia University in collaboration with students and facilities of the Schools of Medicine at Cornell University, the University of Pennsylvania and Western Reserve University. It is the aim of these studies to find out how medical students coming from varied socio-economic, cultural and educational backgrounds emerge as doctors; and why these students exposed to what might at first glance appear to be similar educational experience in medical school, become doctors with different conceptions of their role. In brief, these studies examine by what processes and to what degree the medical school determines the professional-self of the student so that he finally comes to think, feel and act like a doctor.

The first chapter by Robert K. Merton, on the Sociology of Medical Education, is an excellent introduction to the subject and should be read by all medical educators. Here is one sociologist who understands this portion of medical education better than a good many medical educators.

Two chapters consider in some detail the Cornell Comprehensive Care and Teaching Program which is an experiment in medical education designed to do what its name implies. Why do medical students decide to study medicine and how do medical students differ from law students? These questions are dealt with at length with interesting if not conclusive observations.

Students develop new ideas about themselves in the role of physicians and new attitudes toward patients as they progress. They also acquire attitudes toward specialization. These questions are the subject of considerable thought and although it is difficult to draw clear-cut conclusions, the information is certainly worth-while.

One chapter reviews some of the different types of uncertainty which students will encounter and some of the ways he learns to deal with uncertainties. This is a fresh point of view, far different from that which believes we can train medical students to be exact scientists in command of the situation at all times. If medical students could leave medical school with the concept that they will more often than not, be dealing with uncertainties, he might be saved many frustrations and uncertainties of his own.

This book should be very helpful to those learning as well as teaching the social aspects of medicine and should be read by all medical educators.

Chemistry and Biology of Mucopolysaccharides
A Ciba Foundation Symposia

Edited by G. E. W. Wolstenholme and Maeve O'Connor. 313 pages, 48 illustrations. Boston: Little, Brown and Company, 1958. Price $8.50.

This volume is the most recent in a series which has come to be accepted as one of the best sources of information on the current status of important biologic areas. The title is perhaps unavoidably vague, since terminology in this field of carbohydrate containing compounds of physiologic interest is still rather unsettled. In recent years, a considerable revival of interest has been stimulated by the development of newer technics of isolation and characterization. Biochemists, physiologists, pathologists and immunologists have been active and this Ciba Symposium presents in eminently usable form the views and methods of an outstanding group of investigators from these fields. While the major emphasis is given to the chemistry and distribution of sialic acid Klenk, (Gottschalk), blood group substances (Springer, Morgan, Kabat), mucopolysaccharides in connective tissue (Dische, Partridge) and lipopolysaccharides (Westphal), a great deal of emphasis is given over to the problems of general chemistry of mucopolysaccharides (Stacey), physicochemical studies of hyaluronic acid (Ogston), sulfated and neutral mucopolysaccharides (Jeanloz, Dische, Odin, Winzler), biosynthesis of mucopolysaccharides (Dorfman, Cifonelli), and several other topics.

This book is warmly recommended to those interested in advances in our knowledge of the chemistry and biology of these compounds and in their relationship to various disease states. In this latter connection the papers by Winzler on plasma glycoproteins and by Maclagen and Anderson on the colloidal properties of urinary mucopolysaccharides should be of particular interest.

Classification for Medical Literature

By Eileen R. Cunningham, Librarian and Professor of Medical Library Science, Vanderbilt University School of Medicine. Fourth Edition, 164 pages. Nashville, Tennessee: The Vanderbilt University Press, 1955. Price $3.25.

Continued on page 123

Dr. Rouse—SMA's Fifty-Fourth President

MILFORD O. ROUSE, M.D.

Dr. Milford Owen Rouse of Dallas was installed as the 54th President of the Southern Medical Association during the New Orleans meeting, November 3-6. He will preside over the Atlanta meeting November 16-19, 1959.

Dr. Rouse was born in Jacksonville, Texas, August 10, 1902. He spent some of his boyhood in Brazil and Cuba where his parents were Southern Baptist missionaries.

He received his B.A. degree from Baylor in 1922 and his M.A. in 1923. He was a teaching fellow in zoology at Baylor while earning his M.A. degree. He entered the College of Medicine at Baylor in the fall of 1923 and received his M.D. degree in 1927.

Dr. Rouse interned at the Fort Sam Houston Army Hospital in 1927-28 and entered private practice in Dallas as an associate of Dr. H. G. Walcott, a pioneer gastroenterologist. In 1935, Dr. Rouse started the firm of Drs. Rouse and Patterson which is presently a partnership of Drs. Rouse, Cecil O. Patterson, Herbert A. Bailey. F. Clark Douglas and John W. Fisher. He limits his practice to gastroenterology.

Since 1943, he has been clinical professor of medicine (gastroenterology) at Southwestern Medical School in Dallas.

Dr. Rouse is a past president of the Dallas Southern Clinical Society, the Texas Society of Gastroenterologists and Proctologists, and the Texas Medical Association. He is Chairman of the Texas delegation to the American Medical Association and holds membership in many medical societies including the Texas Academy of Internal Medicine, the Texas Geriatric Society, the Dallas Academy of Internal Medicine and the American Gastroenterological Association. He is a diplomate of the American Board of Internal Medicine and of the Board of Gastroenterology and is a fellow of the American College of Physicians.

He joined the Southern Medical Association in 1929—two years after graduation from medical school. He has served the Association in many capacities including the Chairmanship of the Section on Gastroenterology, Councilor from Texas 1950-55 and Chairman of the Council in 1955.

Commenting on the Southern Medical Association he said: "In Southern Medical I have found superb scientific medicine combined with personal friendships of a wide range. My continuous membership has been one of my best investments."

Thus, as the Southern Medical Association honors Dr. Rouse with its highest office, the life, inspiration and leadership of this distinguished churchman, civic leader, physician and medical statesman in turn honors the Southern Medical Association. **VOF**

Highlights of the New Orleans Meeting

The 52nd meeting of the Southern Medical Association, held in New Orleans, November 3-6, was the largest in the history of the Association. The meeting attracted a total of 6,121 registrants of which 3,587 were physicians. The largest previous meeting was the Miami Beach session in 1957 which attracted 6,003 registrants, with 3,235 physicians.

To Dr. Edwin L. Zander, General Chairman, and the more than 300 New Orleans physicians who served actively on various committees go much of the credit for the success of the meeting.

The President's Luncheon

Dr. F. J. L. Blasingame, Executive Vice-President of the AMA, was the President's guest and principal speaker at the President's Luncheon on Monday, November 3. The luncheon was concluded with a brief business session.

Doctor's Day Luncheon — Woman's Auxiliary

The Auxiliary's Doctor's Day Luncheon, held on Tuesday at the St. Charles Hotel was considered the largest and best in history. It featured Doctor's Day Awards to state and county auxiliaries and was concluded with a Mardi Gras pageant in full costume. The Auxiliary reported 895 registrants.

Annual Dinner — President's Night

The Annual Dinner Dance, held in the International Room of the Roosevelt Hotel, was attended by more than 500 persons. It featured the presidential address by Dr. W. Kelly West and the election of officers. A highlight of the session was the conferring of the Distinguished Service Award on Dr. T. W. Moore, retired 92 year old physician of Huntington, West Virginia. Other awards included Scientific Exhibit Awards for first place to Oscar Creech, Jr., E. T. Krementz, Keith Reemtsma, and R. F. Ryan, Tulane Medical School, New Orleans, Louisiana; second place to A. C. Broders, Jr., R. R. White, W. H. Hunt III, N. C. Hightower, Jr., J. C. Stinson, and Henry Laurens, Scott and White Clinic, Temple, Texas; third place to John Moossy and Richard Paddison, Louisiana State University School of Medicine, New Orleans, Louisiana. Golf trophies were awarded to Dr. Fred P. Thomas, Houston, Texas, and Dr. Ruble E. Moor, New Orleans, Louisiana.

The evening was concluded with dancing, featuring two outstanding New Orleans jazz bands. The entertainment was under the direction of Dr. Edmond Souchon.

Medical Student Representatives

The following medical schools were represented by an elected member of each senior class who was a guest of the Association: Baylor University College of Medicine, Louisiana State University School of Medicine, St. Louis University School of Medicine, Southwestern Medical School, Tulane University School of Medicine, University of Arkansas School of Medicine, University of Mississippi School of Medicine, University of Oklahoma School of Medicine, University of Tennessee College of Medicine, University of Texas School of Medicine, Vanderbilt University School of Medicine, and Washington University School of Medicine. Activities for this group included a dinner on Monday evening and a full four day schedule of activities designed to acquaint the students with the full range of a large medical meeting. These "doctors of the future" and Dr. J. B. Cummins, 100 year old member of Southern from Fort Worth, dramatically represented medical practice of the nineteenth and twentieth centuries.

Social Highlights

Social activities galore added spice and color to this greatest of Southern Medical meetings. A highlight of these activities was the reception given for President and Mrs. West on Sunday evening by members of the Oklahoma State Medical Association.

JAPAN

Dr.

Dr. F. J. L. Blasingame, the President's guest, discusses the meeting with Drs. Charles B. Odom, Edwin L. Zander, General Chairman, and President W. Kelly West.

Dr. Hugh Lawson confers the Distinguished Service Award on Dr. T. W. Moore of Huntington, West Virginia.

Dr. West delivers presidential address.

Dr. George F. Lull addresses medical student representatives.

Part of audience—President's Luncheon.

Doctor's Day Luncheon—Woman's Auxiliary.

Speakers' table—Annual Dinner.

The new

Dr. and Mrs.
joy New O

The President's Night audience.

The new President—Dr. Milford O. Rouse.

Dr. and Mrs. Joe Stewart, Miami, enjoy New Orleans jazz at Annual Dance.

Head table—Council Luncheon—Dr. Milford O. Rouse, Mrs. Walker L. Curtis, Auxiliary President, President West, and Council Chairman, Dr. Fount Richardson.

Dr. J. B. Cummins, 100 year old member from Fort Worth, gives medical students some pointers.

Twelve medical school student representatives with their Committee (center), Drs. R. H. Kampmeier, George D. Wilson, and Donald S. Daniel.

Dr. J. B.

Council holds first business session.

Dr. J. B. Cummins discussing geriatrics with Drs. Alton Ochsner and Tom D. Spies, symposium participants.

Partial view of the 213 exhibits—Municipal Auditorium.

THE NEW ORLEANS MEETING

The 52nd Annual Meeting held in New Orleans on November 3-6 attracted 6,121 registrants, including 3,587 physicians, 1,327 ladies, 753 nurses, technicians, exhibitors, visitors and guests, and 454 medical students.

Registered physician attendance by states in the territory of the Southern was as follows:

Alabama	169
Arkansas	70
District of Columbia	58
Florida	208
Georgia	157
Kentucky	120
Louisiana	161
New Orleans and Vicinity	1,256
Maryland	66
Mississippi	130
Missouri	120
North Carolina	132
Oklahoma	83
South Carolina	71
Tennessee	131
Texas	323
Virginia	150
West Virginia	34

Physicians attending from other states and foreign countries were as follow:

Arizona	1
California	6
Colorado	2
Connecticut	4
Illinois	16
Indiana	8
Iowa	1
Kansas	5
Massachusetts	2
Michigan	13
Minnesota	5
New York	23
New Jersey	11
Ohio	14
Pennsylvania	20
Washington	1
Wisconsin	4
Foreign	12

Registrations of the 3,587 physicians by Sections and the attendance at the sessions of the Sections were as follow:

Specialty Designated	No. Registered	Highest Attendance at Section Sessions
Allergy	37	205
Anesthesiology	79	300
Dermatology and Syphilology	137	132
Gastroenterology	45	205
General Practice	337	261
Gynecology	134	280
Industrial Medicine and Surgery	25	50
Medicine	496	200
Neurology and Psychiatry	101	65
Obstetrics	187	275
Ophthalmology and Otolaryngology	214	126
Orthopedic and Traumatic Surgery	213	205
Pathology	57	30
Pediatrics	148	83
Physical Medicine and Rehabilitation	10	22
Proctology	34	44
Public Health	17	35
Radiology	104	70
Surgery	485	200
Urology	74	80
Unclassified	73	
Specialty undesignated	580	
Total physician registration	3,587	

Southern Medical Association
2601 Highland Ave., Birmingham 5, Ala..

Application for Membership

I desire to be enrolled a member of the Southern Medical Association (which includes subscription to the Southern Medical Journal) for which I enclose $10.00 to pay for the first year's dues, membership to continue until otherwise instructed (dues payable in advance).

I am a member in good standing of the ..... County and ..... State Medical Societies.

Former member of Southern Medical Association? Yes ☐ No ☐

Name (please print) .....

Street or Office Address .....

City ..... Zone ..... State .....

Specialty (if any) ..... Date of Birth ..... School .....

Date ..... Signature ..... M.D.

MEMBERSHIP—The membership of this Association shall be limited to eligible members of the various state and local medical societies of the following states, viz.: Alabama, Arkansas, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, Missouri, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia, and Medical Officers of the United States Army, Navy, Public Health Service and Veterans' Bureau on active duty, and American members of Canal Zone Medical Society and the Puerto Rico Medical Association.

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BOOK REVIEWS

Continued from page 112

The publication of the 4th edition of the Cunningham *Classification for Medical Literature* is welcomed by both medical librarians and physicians. As in previous editions, the 26 main sections cover the preclinical sciences, the various systems of the body, and the general disciplines, arranged to conform to the curriculum and subject sequence of medical teaching.

Under each organ and system of the body, and under a disease or group of diseases, can be found all of its aspects—anatomy, physiology, pathology, etc.

The system used is a capital letter followed by an arabic number, then a small letter, providing a flexible and easily expandable scheme.

Nonmedical and related subject fields are covered in the supplementary section which uses a double capital letter and is subdivided by the same method of alternating letters and figures.

A major change in this edition has been made in the "G" section dealing with Psychology and Psychiatry. In these areas certain sections have been rearranged and regrouped in order to bring related material together.

Other changes have been made in S7x, Tumors, and in Y2—, Radiation and Radioactivity, Roentgenology.

Considerable expansion of the index in this edition has been made and terminology throughout has been brought up to date.

Physicians who are searching for a logical system by which to file their personal collections will find this classification a splendid scheme, since it can be used for books, monographs, reprints, and other types of publications designed for subject arrangement.

The Riddle of Stuttering

By C. S. Bluemel, M.D., Mount Airy Sanitarium, Denver, Colorado. 139 pages. Danville, Ill.: The Interstate Publishing Co., 1957.

Dr. Bluemel's treatment of the problem of stuttering—or "stammering," to use the term preferred by the author—is an insightful one, despite certain structural and theoretical weaknesses.

Distinctions are made between stammering, stuttering, neurotic nonfluency and hysterical stammering. Stammering, considered to be a psychoneurotic phenomenon, differs from other neuroses only in that it can be "conspicuously seen and heard." "A complex disorder of speech and personality," stammering involves fear conditioning, and is a chronic condition demanding clinical attention. Contrary to the usage of many American workers, Bluemel affixes the term stuttering to the developmental hesitancies of childhood speech. These are the "unorganized," relatively nonchaotic expressions of childhood, where an immaturity of physiologic mechanisms are obtained. Neurotic nonfluency is a prostammering phenomenon seen in children who are hyperkinetic, excessively tense and easily disrupted emotionally. Hysterical stammering is only one expression of a hysteric personality, the speech disturbance of which is transient.

This use of terminology, while not exclusively Bluemel's, may cause some consternation in the Johnsonian camp. These clinicians do not approve of the application of negatively-toned labels to so-called "normal" hesitancies of childhood speech. While not an important issue in and of itself, the semantics involved have theoretical significance for those who do endorse Johnson's "diagnosogenic" theory of stuttering. Bluemel's acceptance of Johnson's theory is only partial. Bluemel's theoretical position lacks research substantiation and because of this his treatise will be subject to much criticism.

Bluemel outlines a program of therapy in which the establishment of "good verbal thinking" is a basic, guiding principle. The stammerer is guided through ear training procedures, and a "psychologically sound" program of sensory re-education is followed. In this, the stammerer learns to "think fluently" before making speech attempts directly. The aim is to carry the stammerer through a series of re-educative steps of graduated difficulty in which speech trials become more explicit and propositional.

Psychotherapy and chemotherapy are recommended when appropriate, though the latter is used adjunctively, primarily. The therapeutic procedures outlined by Bluemel may be self-administered or entrusted to a competent speech therapist. This is enigmatic in view of the speech therapist's almost antithetical stand on the problem. Because of this, their willingness to accept Bluemel's propositions is apt to be half-hearted.

Serious theoretical flaws reduce the over-all tenability of the Bluemel position and his program of therapy lacks verification. However, the lack of validity checks upon therapeutic regimens in stuttering is not a weakness unique to the Bluemel approach. It is a serious shortcoming of all of the major orientations to the problem. Over a period of time, clinical usefulness and research verification remain the ultimate criteria in the evaluation of the Bluemel position.

Physics for the Anaesthetist

By Sir Robert MacIntosh, D.M., F.R.C.S.E., F.F.A.R.C.S., M.D., Nuffield Professor of Anaesthetics, University of Oxford; William W. Mushin, M.A., M.B., B.S., F.F.A.R.C.S., Professor of Anaesthetics, Welsh National School of Medicine; and H. G. Epstein, M.A., Ph.D., F.F.A.R.C.S., Nuffield Department of Anaesthetics, University of Oxford. Second Edition, 431 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $15.50.

This is the second edition of a book written for anesthetists describing principles of physics that relate to anesthesia. It is the announced intention of the authors to produce a work simple enough for anesthetists who are not physicists to comprehend. Care is taken with definitions to make them simple and understandable rather than scientifically precise. After definitions and statements of principles, the significance of these in relation to anesthesia and their applications are described. Having these relationships plainly pointed out makes a knowledge of the principles better appreciated and more easily understood and remembered. Numerous diagrams and illustrations are presented perhaps to an excessive degree. In spite of the announced intention for simplicity, in places descriptions and mathematical formulas are encountered in more detail than will be of interest to the average anesthetist. This is illustrated in the new chapter on pressure reducing valves.

Approximately 25 per cent of this new edition is devoted to four chapters on explosions. This is a subject of great interest to anesthetists and is covered in great detail. However, a greater proportion of space is devoted to this topic than would appear to be necessary.

This new edition is a welcome revision to the first edition published in 1946. It remains one of the few textbooks on physics related to anesthesia and written for anesthetists and, as such is a useful component of the anesthesia library.

The Treatment of Fractures

By Lorenz Bohler, M.D., Director of the Accident Hospital, Vienna XX; Professor of Accident Surgery, University of Vienna. Translated by Alfred Wallner, M.D., and Otto Russe, M.D. Volume 3. 2,297 pages. 1,699 illustrations. New York: Grune and Stratton, 1958. Price $21.00.

This is the third volume of the current edition of *The Treatment of Fractures* written by Dr. Lorenz Bohler. Unfortunately, the book, like the two preceding volumes, loses a great deal of its value because of the verbosity of the author, the plethora of photographs and illustrations, and the repetition. The author's experience in the treatment of fractures is unexcelled. He is a critical observer of his own results and appears ever ready to change and incorporate improved methods in his methods. It cannot be denied that this is a useful book because virtually all types of fractures are considered. The entire volume is devoted to injuries of the knee joint, leg, ankle and foot. One must admire the tremendous effort on the part of the author to utilize this vast array of material, however, he seems to use it only too well. There have been in the first three volumes a total of 3,098 figures and, as one would expect, there are not infrequent mistakes in the author's reference to this multitude of figures. One's everlasting hope is, with the expectation of possibly two more volumes to complete the present edition, that the author could reduce his verbage to no more than two volumes. This could be done with almost no sacrifice of the points which Dr. Bohler wishes to make.

Your Speech Reveals Your Personality

By Dominick A. Barbara, M.D., 167 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $5.50.

Speech is the man. With this stereophonic approach to his subject, Dr. Dominick A. Barbara, the New York psychoanalyst, in his latest work, *"Your Speech Reveals Your Personality,"* picks up man talking everywhere, anytime. He listens to the bleat of the submissive, the bellow of the mastery-seeker, the grunt of the resigned. He bends a marvelling ear at man's infinite virtuosity in mutilating the clear score of objective reality. For neurotic man is always playing to the house and he must always sound with the golden tones of impossible perfection. He must have his audience always on its feet for the particular virtues esteemed in his neurotic structure—for his sweetness, for his strength, for his magnificent indifference. The object is self-glorification but the end is something else. To achieve his goal man must add false and extra notes, render the minor events of life with hysterical bravura or the major crises with hushed pianissimo. The result is the fool, the braggart, the milquetoast. Man's neurotic search for magnificence accounts, moreover, for a host of his language and speech problems. Viewing the word as the chief source of his self-enhancement or self-destruction, man endows it with magical properties. It can make him or break him. Thus, the stutterer, having experienced a nonfluency with a certain set of symbols, superstitiously avoids same in the future. But in his struggles out of the verbal traps through head jerks, grimacing, etc., he creates a far more unpleasant impression than with the relatively short block itself. The schizophrenic, ducking reality, becomes unintelligible as he creates characteristic neologisms.

But what is the cure for these problems? According to Dr. Barbara, applying principles of the late Dr. Karen Horney, man must rid himself of his phoney, "phantom" role and return to his core, the real self, facing the world as it really is, not as he might wish it to be, and dealing with same in realistic terms. Such a wide-lensed view of speech makes this text valuable background reading for a score of specialties.

Fundamentals of Electrocardiography and Vectorcardiography

By Lawrence E. Lamb, M.D., Director of Cardiology and Chief, Department of Internal Medicine, Air University School of Aviation Medicine, USAF, Randolph Air Force Base. 138 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $9.50.

Dr. Lamb has written a practical book on the fundamentals of vectorcardiography which is designed for both the beginner and for those clinicians with specialized interest in this field.

After a review of the fundamental vector concepts, with clear mathematical and physical illustrations, the processes of depolarization and repolarization of the heart are discussed. The normal electrocardiogram and vectorcardiogram are presented with an excellent, easy to interpret, chart of the spatial QRS-T angle which should save the cardiologist considerable time.

The abnormal vectorcardiogram and the changes produced by chamber enlargement, conduction defects, pericarditis, and myocardial infarction are concisely illustrated and should be easily understood by the beginner.

In conclusion, the influence of drugs, electrolyte disturbances, and the various arrhythmias are adequately included in this practical book, which is most timely since the physician needs a basic foothold in this sometimes complex approach to cardiology.

Physical Diagnosis

By F. Dennette Adams, M.D., Physician, Board of Consultation, Massachusetts General Hospital. Fourteenth Edition, 879 pages. Baltimore: The Williams and Wilkins Company, 1958. Price $12.00.

Cabot's book on Physical Diagnosis, first published in 1900, remained for many years the classic textbook on physical diagnosis in this country. For its twelfth edition, in 1938, Dr. Adams joined Dr. Cabot in continuing this classic work. The two editions preceding

the present appeared under the present author's name and now the new edition.

As one compares the present volume with Cabot's sixth edition, as was used by this reviewer as a student, one appreciates the extension of the diagnostic aids which have evolved over the years, though physical diagnosis has changed but little insofar as its technics are concerned.

Thus the present volume is more than a textbook in physical diagnosis; it actually represents diagnosis in medicine, surgery and almost all other fields of medicine. The ancillary aids of the electrocardiogram and the x-ray are extensively used to amplify the discussions.

This is an excellent reference book for the undergraduate in his third year clinical clerkship, the fourth year student and, likewise, has a valuable place on the shelf of the practitioner's library. Since it is actually more than a book on physical diagnosis, it may provide a diet too rich for the second year student who is embarking on the sea of physical diagnosis *per se*, and who must be taught to chart his course by the use of his senses before he calls upon additional aids in his navigation. This is all a matter of philosophic outlook.

Functional Bracing of the Upper Extremities

By Miles H. Anderson, Ed.D., Director, Prosthetics Education Project, University of California School of Medicine. Edited by Raymond E. Sollars. 463 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $9.50.

Here is a useful book of particular value to the orthotist and the prosthetist and of more limited value to the occupational therapist, the physical therapist, and to the orthopedic resident. It will be of little value to the practicing orthopedic surgeon.

The book is broken down into units rather than chapters. Unit A is concerned with the functional anatomy of the hand. This is a very accurate and concise discussion of hand anatomy, useful to the prosthetist or orthotist. It, of course, has no value to the surgeon. The remaining units are concerned with assistive hand splints, feeders, special assistive devices, functional arm braces and shoulder braces. There is a second unit concerned with the basic anatomy of the arm and shoulder. The illustrations are rather profuse and, in general, are well reproduced. Where indicated diagrams are used. The discussions on the actual technic of making braces is very good, and I am sure were found to be most useful by the orthotists. It is most convenient to have within one cover the technical description of how to fabricate so many useful splints, and therein lies the great value of this book.

Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death

1955 revision. Volumes 1 and 2, 393 and 540 pages. World Health Organization, 1957. New York: Columbia University Press, 1958. Price $6.75 (both volumes).

These volumes published by WHO give the seventh decennial revision of the standard international system of classification for causes of death. This is the system used in vital statistics tabulations of death certificate data. It can be used with disease and injury records, but is to be distinguished from the more specific nomenclature for medical diagnoses commonly used in U. S. hospitals, the *Standard Nomenclature of Diseases and Operations*. The present revision has only minor changes from the sixth revision. Provision is made for more detailed classification of neoplasms by site. Rules for selection of the underlying cause of death from a multiplicity of reported causes have been somewhat modified and made more precise. *The International Statistical Classification* is not satisfactory in all its sections, notably in its classification of mental psychoneurotic and personality disorders. However, improvements will continue to be made as clinical concepts and terminology evolve. All doctors should be familiar with the basic principles of nomenclature and statistical classification of diseases and causes of death, and anyone utilizing vital statistics data should read the introduction to volume 1, and the Rules for Classification.

Sherrington, Physiologist, Philosopher and Poet

By Lord Cohen of Birkenhead, M.D., D.Sc., LL.D., F.R.C.P., F.A.C.P., F.F.R., F.S.A., J.P., Professor of Medicine in the University of Liverpool. 108 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $3.50.

This is an excellent example of the short but comprehensive biography done so well by British men of letters. Lord Cohen has culled the meat from the tremendous life and works of Charles Sherrington in such a fashion as to make this work a must in any library. Sherrington's 95 years and 320 publications would make such a task terrifying. The ease and clarity with which the neurophysiological material is summarized will engender admiration in scientific circles. Sherrington's literary efforts are slightly less impressive but Cohen has picked out passages of prose and portions of poetry which add further luster to the life of this most remarkable man.

Orthopedic Diseases
Physiology-Pathology-Radiology

By Ernest Aegerter, M.D., Professor and Director of the Department of Pathology, Temple University School of Medicine and Professor of Orthopedic Pathology, University of Pennsylvania Graduate School of Medicine; and John A. Kirkpatrick, Jr., M.D., Assistant Professor of Radiology, Temple University Medical Center. 588 pages. Philadelphia: W. B. Saunders Company, 1958. Price $12.50.

In a single volume, a pathologist and a radiologist have collaborated to present an excellent work on orthopedic diseases. The authors, while admitting the book is not complete, have sifted and presented the available literature in a remarkably concise and readable manner. The first section, composed of six chapters, is presented as a review of the anatomy, physiology and cystology as well as the radiology of the skeletal system. In the second section is presented disturbances in the skeletal development. In section three, disturbances in the normally formed skeleton are discussed and, in chapter four, tumor and tumor-like processes are presented. All of these sections are

well organized and the material is made readily available by an adequate index. Also, the bibliography is presented at the end of each chapter so that one may readily expand his knowledge by examining the references. This is made even easier since the authors have broken down the references in the bibliography very carefully into subject material. The book is highly readable, a trait singularly lacking in the voluminous and often verbose American literature. One can be certain that this book will find an extensive reading public among medical students, orthopedic, radiology and pathology residents, as well as among the active practitioners in these fields.

Infectious Diseases of Children

By Saul Krugman, M.D., Associate Professor of Pediatrics, New York University College of Medicine; and Robert Ward, M.D., Professor and Head of the Department of Pediatrics, University of Southern California. 330 pages with 44 illustrations and 7 color plates. St. Louis: The C. V. Mosby Company, 1958. Price $10.00.

This is an excellent, concise description of the infectious diseases of children and their variation in various age groups. Included is a chapter on care of the communicable diseases in the hospital and the home. The chapters on Coxsackie, adeno-virus, and staphylococcal infections are very timely and very well done, covering a lot of information succinctly. The illustrations are few in number but very good. References following each chapter appear to be well chosen and not excessive in number. The antibiotics are discussed individually with the diseases in which their use is appropriate and not together as a separate chapter. This contributes to the brevity and effectiveness of the book.

This book is highly recommended for students and for physicians dealing with children.

Communicable Diseases. A Bibliography of Internal Medicine

By Arthur L. Bloomfield, M.D. 560 pages. Chicago: The University of Chicago Press, 1958. Price $10.00.

The author of this book, despairing at the utter impossibility of keeping up with current medical literature, to say nothing of the student or practitioner acquiring even a superficial knowledge of the history of disease, points out that "few medical students nowadays (1957) remember Sir Thomas Lewis, George Minot, or F. G. Banting; most of them never heard of Von Mering and Minkowski." He correctly points out that in this day of Specialty Board examinations the student tends to keep up with the new, the esoteric and the curious at the expense of the fundamental and historical. How often does modern clinical teaching concentrate on minutiae and details neglecting broad knowledge historically oriented!

Dr. Bloomfield set out to help repair this gap in medical teaching by preparing selected bibliographies listing important contributions of nineteenth and twentieth century medicine which he hoped would stimulate the interest of students in the events which led up to present concepts of communicable diseases. The first of these on typhoid fever appeared in 1932. and since then thirty others dealing with the most common communicable diseases have been published. This book is a collection of these thirty-one articles. The author has read nearly every reference himself and summarized each briefly so that the book is a ready source of major contributions to modern medical knowledge. The work is not meant to be a complete bibliography, rather a selected one. The selection of the single "most important" article on some aspect of a particular disease is a most difficult thing to do and there will undoubtedly be some differences of opinion regarding references both those omitted and those included.

In a work of this type the experience and judgment of the compiler will influence the selection. The author points out that he has prepared a bibliography primarily for clinicians rather than for specialists. This should certainly explain why some equally important but less clinically oriented references may not appear. He might have added that the book is for students too, because it is admirably suited for the medical student who may not know how or where to find original material about a disease.

Dr. Bloomfield, a great contemporary teacher and clinician, is exceptionally well-qualified to perform the task he has set himself. His book will be invaluable for the libraries of medical schools, clinicians and students, not only those with a cursory knowledge, but also those who might have an enthusiastic liking for medical history.

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1. Doe, J. E.: What You Should Know about It, New England J. Med. 243:435, 1950.

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1. Alexander, L.: Chemotherapy of depression—Use of meprobamate combined with benactyzine (2-diethylaminoethyl benzilate) hydrochloride. J.A.M.A. 166:1019, March 1, 1958. 2. Current personal communications; in the files of Wallace Laboratories.

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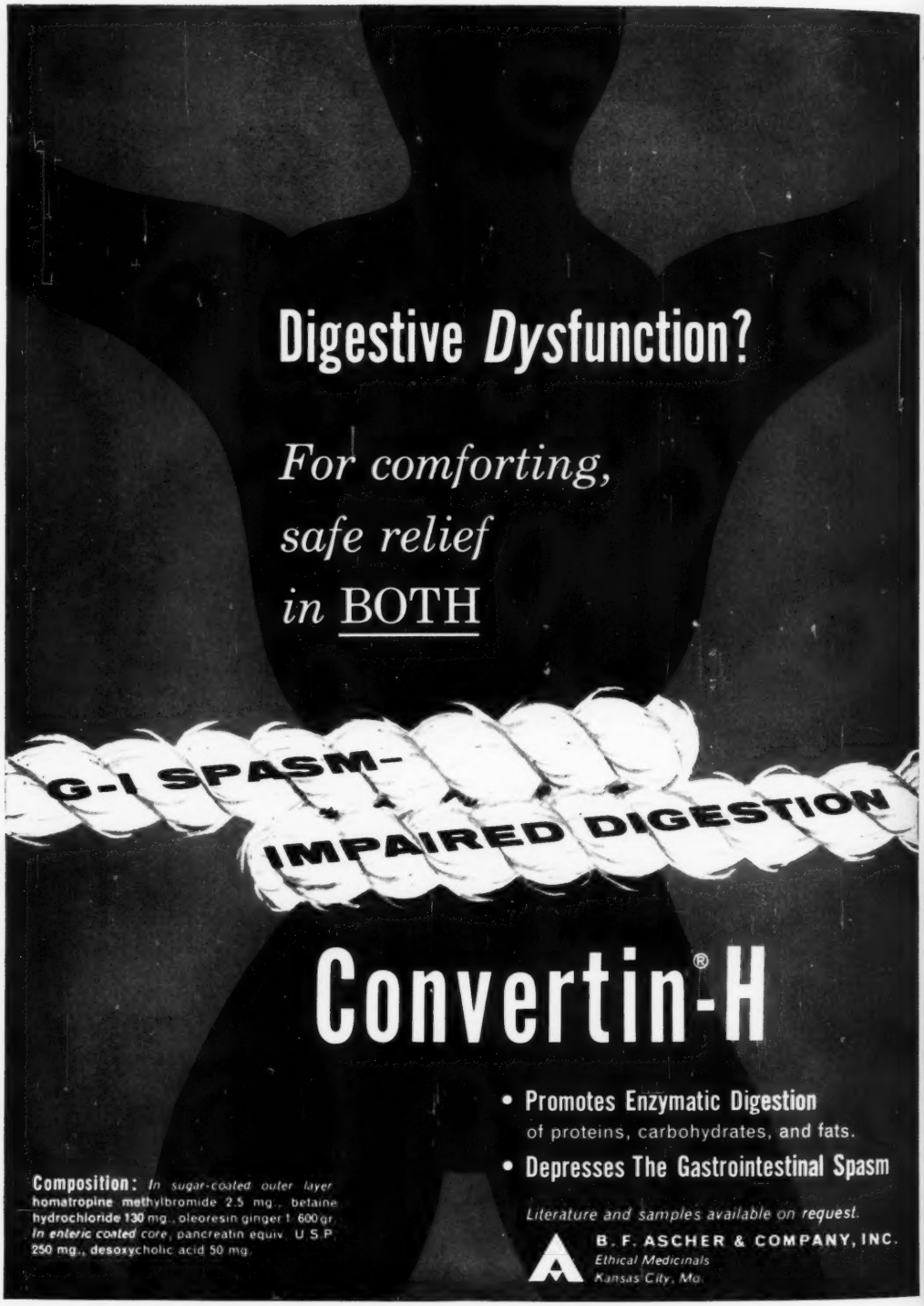
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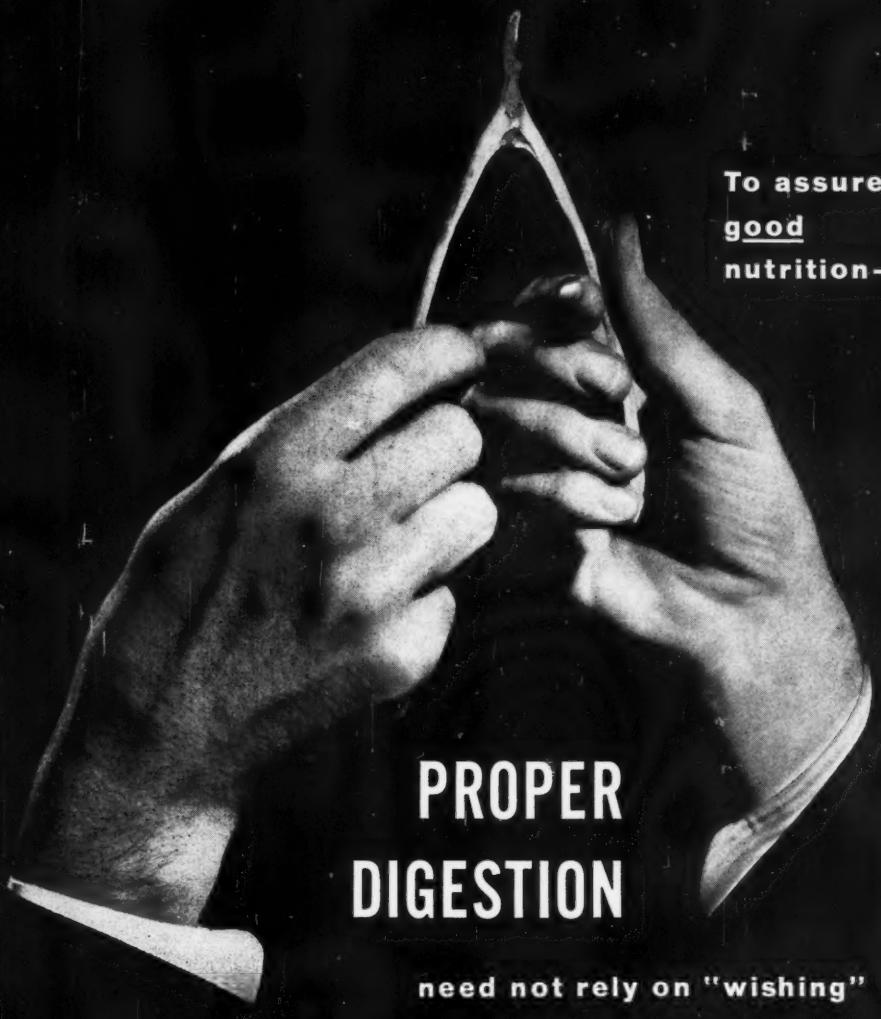

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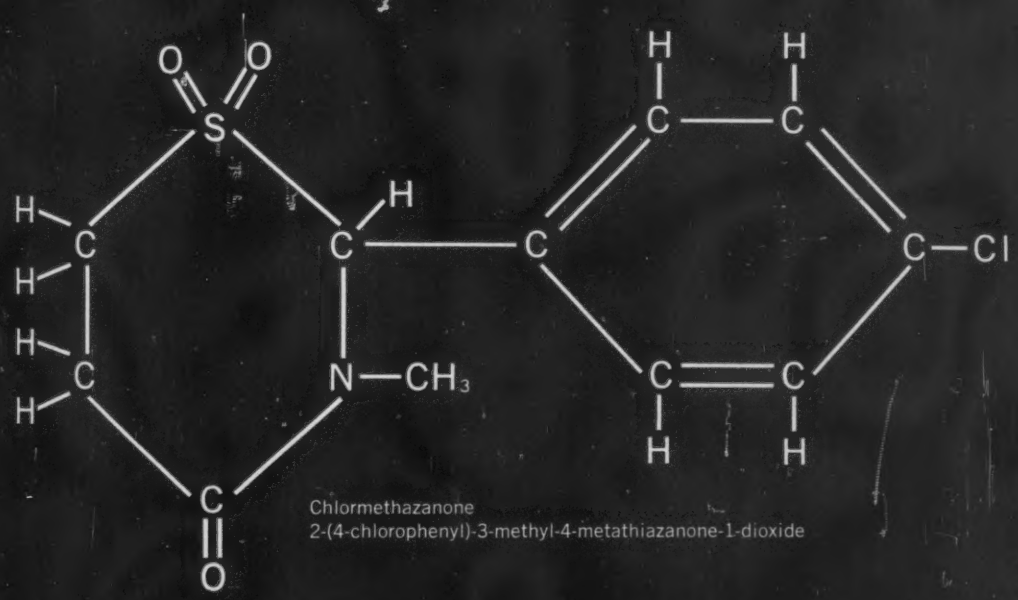


Chlormethazanone
2-(4-chlorophenyl)-3-methyl-4-metathiazanone-1-dioxide

unrelated chemically to any other drug in current use

designed to be equally effective as both

a MUSCLE RELAXANT

a TRANQUILIZER

Trancopal

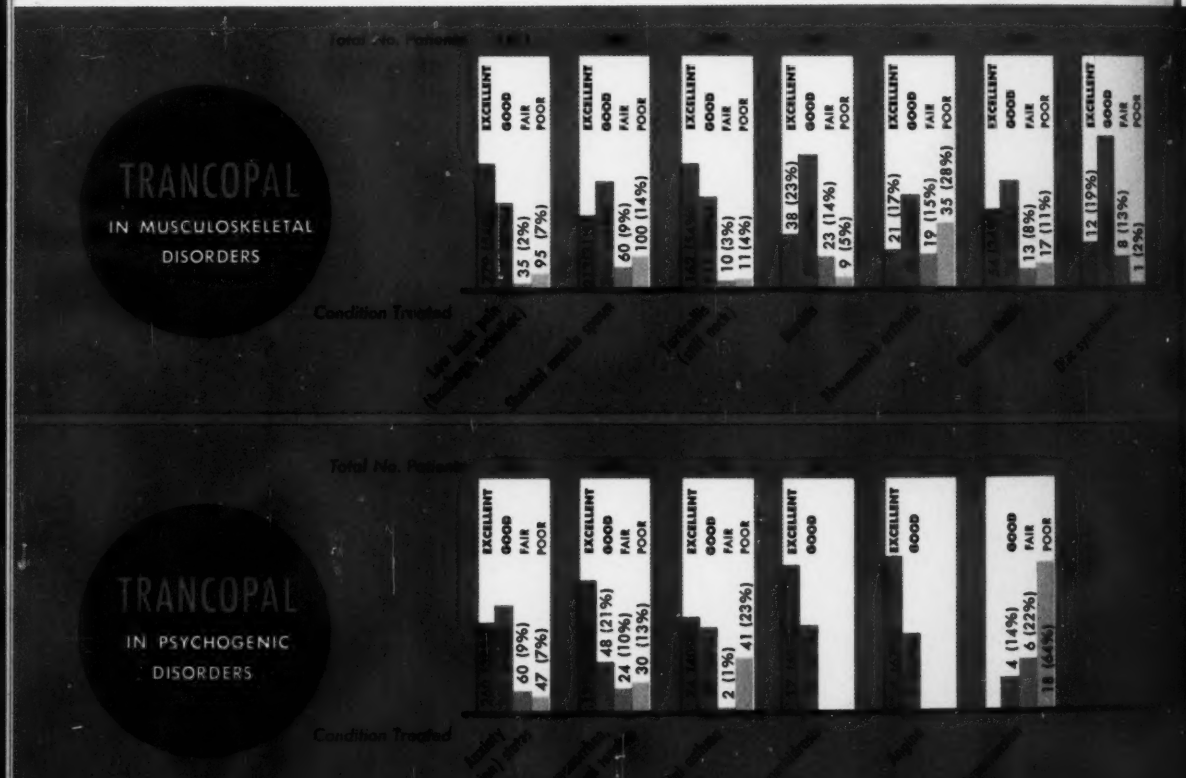
*the first true "TRANQUILAXANT"**

offering new freedom for your patients... from muscle spasm, from tension and anxiety, from side effects

* **tran-qui-lax-ant** (tran'kwi-lak'sant) [< L. tranquillus, quiet; L. laxare, to loosen, as the muscles]

EXCEEDS OLDER DRUGS UP TO 4 TIMES IN PERCENTAGE OF CLINICAL EFFICACY (Lichtman)

The results of clinical studies of over 4000 patients by 105 physicians demonstrate that TRANCOPAL often is effective when other drugs have failed. From these studies it is clear that TRANCOPAL probably can provide more help for a greater number of tense, spastic, and/or emotionally upset patients than any other chemotherapeutic agent in current use.



TRANCOPAL... the first true "tranquilaxant"

Both a muscle relaxant and a calmative agent.

In musculoskeletal disorders, 91 per cent effective.

In anxiety and tension states, 93 per cent effective.

Lower incidence of side effects than with zoxazolamine, methocarbamol or meprobamate.

No known contraindications. Blood pressure, pulse rate, respiration and digestive processes unaffected by therapeutic dosage. No effects on hematopoietic system or liver and kidney function.

Low toxicity. In animals, even less toxic than aspirin.

No gastric irritation. Can be taken before meals.

No clouding of consciousness, no euphoria or depression.

No perceptible soporific effect, even in high dosage.

CLINICAL RESULTS IN 4092 PATIENTS**

MUSCULOSKELETAL CONDITIONS
2929 Patients

+

PSYCHOGENIC CONDITIONS
1163 Patients

=

TOTAL 4092 Patients

MAJOR IMPROVEMENT
84%

**Cooperative Study, Department of Medical Research, Winthrop Laboratories.

designed to be equally effective as both

a MUSCLE RELAXANT

a TRANQUILIZER

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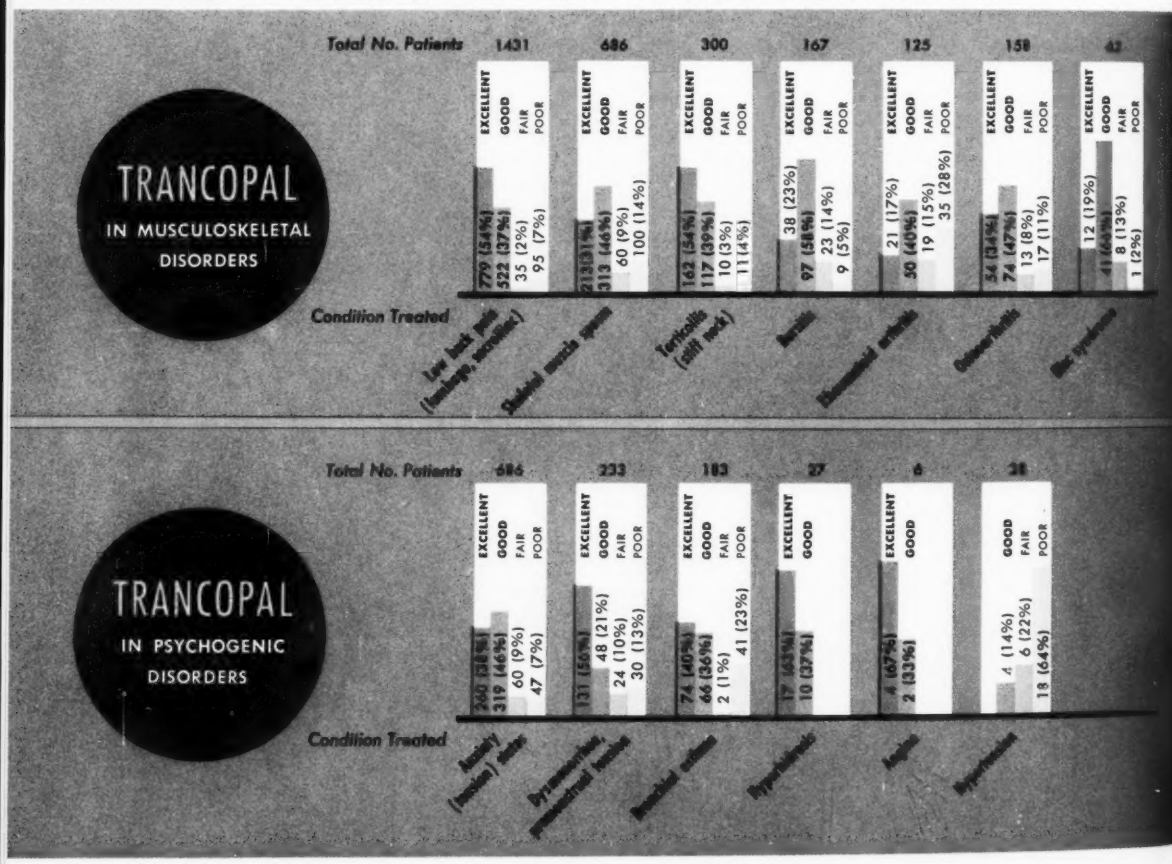

TRANCOPAL [redacted] the first true "tranquilaxant"

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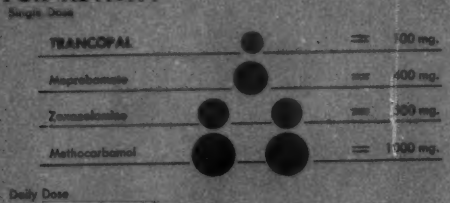
**Cooperative Study, Department of Medical Research, Winthrop Laboratories.

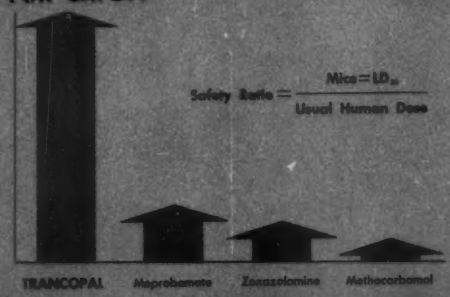
Compare Trancopal with 3 widely used central relaxants

FOR ACTIVITY



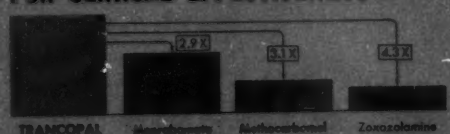
Considering the usual human dose, Trancopal, the first true "tranquilaxant," is four to ten times as potent per milligram.

FOR SAFETY



Comparative pharmacologic tests showed that Trancopal is up to thirteen times as safe, or up to thirteen times less toxic. The measure of safety was the LD_{50} in mice/usual human dose.

FOR CLINICAL EFFECTIVENESS



A clinical comparison in low back pain, torticollis, bursitis and anxiety states showed that Trancopal is up to four times as effective. Each of 40 patients received all four drugs in random rotation for several days. While each of the four drugs gave some relief, only the one providing the most effective relief was recorded.

INDICATIONS

Musculoskeletal
- Low back pain (lumbago)
- Neck pain (torticollis)
- Bursitis
- Rheumatoid arthritis
- Osteoarthritis
- Disc syndrome
- Fibrositis
- Joint disorders (ankle sprain, tennis elbow, etc.)
- Myositis
- Postoperative myalgias

Psychogenic
- Anxiety and tension states
- Dysmenorrhea
- Premenstrual tension
- Asthma
- Emphysema
- Angina

Neurologic
- Muscle spasm in paralysis agitans, multiple sclerosis, hemiplegia, poliomyelitis

TRANCOPAL thoroughly evaluated clinically

"In the treatment of conditions associated with skeletal muscle spasm there was a high percentage of satisfactory results (excellent, good or fair) in 310 patients (94%) out of 331 treated . . . In 120 patients with simple anxiety or tension states results were satisfactory in 114 (95%). Dosage of chlormethazanone in all cases was 100 mg. t.i.d. As well as relieving the anxiety or tension state, chlormethazanone also allowed these patients to resume their usual occupations."
(Lichtman)

"The effect of this preparation in these cases [skeletal muscle spasm] was excellent and prompt . . ."

Trancopal ". . . was effective in relieving the symptoms of anxiety . . . [with a] profile of pharmacologic actions similar to meprobamate . . ."
(Mullin and Epifano)

"We have just started using it [Trancopal] for relaxing spastic musculature and are very much encouraged."
(Baker)

Trancopal

the first true "TRANQUILAXANT"

Dosage: One Caplet (100 mg.) orally three or four times daily. Relief of symptoms occurs in fifteen to thirty minutes and lasts from four to six hours.

Supplied: Trancopal Caplets® (scored) 100 mg., bottles of 100.

Winthrop Laboratories • New York 18, N. Y.

• Baker, A. B.: Modern Med. 26:140, April 15, 1958. • Cohen, A. I.: In preparation. • Cooperative Study, Department of Medical Research, Winthrop Laboratories. • Gosler, R. M., and Coulter, Toxicol. & Appl. Pharmacol. To be published. • Gosler, R. M., and Surrey, A. R.: J. Pharmacol. & Exper. Therap. 122:24A, Jan., 1958. • Gosler, R. M., and Surrey, A. R.: J. Pharmacol. & Exper. Therap. 122:617, April, 1958. • Lichtman, A. L.: Kentucky Acad. Gen. Pract. J. 4:28, Oct., 1958. • [illegible] W. G., and Epifano, Leonard: To be published. • Surrey, A. R.; Webb, W. G., and Gosler, R. J. Am. Chem. Soc. 80:3469, July 5, 1958.

Printed in U. S. A. 11-58

over 36 females
and over 13 males
in every 1,000
are chronically
constipated*

3 physiologic -way action
CHOLERETIC
DIGESTANT
LAXATIVE
for treating
chronic constipation

CAROID AND BILE SALTS TABLETS act to restore the normal pattern of elimination. Bile salts help overcome the biliary stasis so common in the chronically constipated; Caroid, a potent enzyme, increases protein digestion as much as 15%; and mild laxatives improve peristaltic rhythm and tone—keep stools soft and well formed.

*Modern Medicine Topics, vol. 19, no. 7 (July) 1958.

Caroid® and Bile Salts Tablets

RESTORE REGULARITY WITHOUT IRRITATION, GRIPING OR FLATULENCE

SAMPLES ON REQUEST

AMERICAN FERMENT CO., INC. • 1450 Broadway • New York 18, N. Y.

Continued from page 110

Associate Professor in the Departments of Physiology and Medicine.

ARKANSAS

Dr. Philip P. Ellis, formerly of the State University of Iowa, has been appointed Associate Professor to head the Ophthalmology Division in the Department of Surgery at the University of Arkansas Medical Center.

Dr. T. E. Williams, Newport, has been elected to membership by the American Board of Abdominal Surgery.

Dr. Samuel A. Corson, Associate Professor of Physiology and Pharmacology at the University of Arkansas Medical School, was one of the three American medical scientists who made a month's visit to the Soviet Union recently. Dr. Corson studied Russian advances in the fields of conditioned reflexes and psychomatic physiology.

Dr. Elisha M. Gray, Mountain Home, Dr. Noah E. Fraser, Conway, Dr. C. A. Henry, Booneville, Dr. Mark Anderson Shelton, Wabbaseka, and Dr. Don Carlos Carter, Parkins, were all honored recently by the University of Tennessee Medical Units for the services they have rendered to their communities during the half-century since their graduation from the University in 1908.

Paul L. Day, Ph.D., Head of the Department of Biochemistry and Assistant Dean, Graduate School, University of Arkansas School of Medicine, has been appointed Scientific Director of the U. S. Food and Drug Administration.

DISTRICT OF COLUMBIA

Dr. Frederick Y. Donn has been awarded a five year certificate in recognition of his excellent work at the McCluer Tumor Clinic at the Alexandria Community Health Center by the American Cancer Society.

Drs. David M. French, John P. Gallagher, Frederick B. Hartsock, William R. Hyde, John J. Kuhn, Philip H. Philbin, Mitchell W. Spellman, and James R. Thistlethwaite, of the District Medical Society, have been inducted into fellowship by the American College of Surgeons.

Dr. Desmond S. O'Doherty has succeeded Dr. Francis M. Forster as Professor and Director of the Department of Neurology at Georgetown University School of Medicine. Dr. Forster recently resigned from the faculty of Georgetown to become Chairman of the Department of Neurology at the University of Wisconsin.

The Women's Medical Society announces that Dr. Inez Edith Wilber is now President, succeeding Dr. Lois I. Platt, who resigned. Other officers include: President-Elect, Dr. Alma Jane Speer; Corresponding Secretary, Dr. Aurora F. Alberti; Recording Secretary, Dr. Bertha E. VanGelderen; and Treasurer, Dr. Dorothy Donley Dowd.

Major General Oliver K. Niess has taken over the post of Surgeon General of the United States Air

Continued on page 52

Now—All cold symptoms can be controlled

Provides Triaminic for more complete and more effective relief from nasal and paranasal congestion because of systemic transport to *all* respiratory membranes—without drawbacks of topical therapy.†

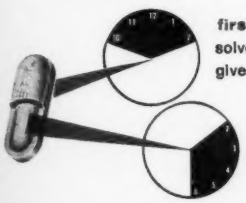
Provides well-tolerated APAP (N-acetyl-p-aminophenol) for prompt and effective analgesic and antipyretic action to make the patient more comfortable.

Provides Dormethan (brand of dextromethorphan HBr) for non-narcotic antitussive action on the cough reflex center in the medulla—as effective as codeine but without codeine's drawbacks.

Provides terpin hydrate, classic expectorant to thin inspissated mucus and help the patient clear the respiratory passages.

†Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. Fabricant, N. D.: E. E. N. T. Monthly 37:460 (July) 1958. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

Special "timed release" design



first—the outer layer dissolves within minutes to give 3 to 4 hours of relief

then—the inner core releases its ingredients to sustain relief for 3 to 4 more hours

also available for those patients who prefer liquid medication: **Tussagesic suspension**

Each TUSSAGESIC tablet provides:

TRIAMINIC®	50 mg.
(phenylpropanolamine HCl	25 mg.
pheniramine maleate	12.5 mg.
pyrilamine maleate	12.5 mg.)
Dormethan (brand of dextromethorphan HBr)	30 mg.
Terpin hydrate	180 mg.
APAP (N-acetyl-p-aminophenol)	325 mg.

Dosage: One tablet in the morning, midafternoon and in the evening, if needed.

Tussagesic* *timed-release tablets*

**Contains TRIAMINIC to STOP running noses and open stuffed noses orally*

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska • Peterborough, Canada

Continued from page 50

Force. He succeeds Major General Dan C. Ogle, who retired after almost 30 years' active service.

The Board of Trustees of the University of Illinois College of Medicine, Chicago, has approved the appointment of Arnold V. Wolf, Ph.D., Walter Reed Army Institute of Research, as head of the Department of Physiology at the College.

GEORGIA

Dr. Francis W. Fitzhugh has been chosen President of the newly organized Grady Hospital Clinical Society, composed of former interns and residents of Grady. Other officers are: Dr. John R. McCain, Secretary, and Dr. J. R. Amerson, Treasurer, all of Atlanta.

Dr. Donald S. Bickers, Atlanta, has been re-elected Secretary-Treasurer of the Southern Electroencephalographic Society.

Dr. William A. Smith, Atlanta, has been made a Diplomate of the American Board of Ophthalmology.

KENTUCKY

Dr. Garnett J. Sweeney, Liberty, has been unanimously elected Chairman of the Kentucky State Medical Association Council. Dr. Sweeney is a former President of the Kentucky Chapter, American Academy of General Practice. He succeeds Dr. Walter O'Nan, Henderson, who was re-elected Councilor from the 2nd District by the House of Delegates. Dr. Carlisle Morse, Louisville, was elected Vice-Chairman of the Council. Dr. Morse is also Governor for Kentucky of the American Diabetes Association and Chairman of the Jefferson County Medical Society Legislative Committee.

Two Kentucky physicians have been honored by the Kentucky State Medical Association for their outstanding work. Recipient of the Outstanding General Practitioner Award was Dr. Brent Weddle, Somerset, for his many contributions to the health, care, education, and welfare of his community. Dr. Joseph E. Johnson, South Williamson, was awarded the Distinguished Service Award for his efforts to enact health legislation in the public interest.

Fifteen Kentucky physicians were accepted recently as fellows of the American College of Surgeons at a meeting of the ACS in Chicago. New fellows include: Drs. L. Douglas Atherton, Thomas E. Booth, Walter I. Hume, Jr., and Bernard J. Schoo, all of Louisville; James A. Harris, William H. Hyden, Samuel W. Lykins, Andrew M. Moore, and Harold Redd, Jr., all of Lexington; Walter R. Johnson, Jr., Paducah; Paul H. Klingenberg, Covington; Joseph H. Krakauer, Middlesboro; Joseph E. Stephenson, Ashland; Hugh C. Williams, Carrollton; and Herman A. Ziel, Jr., Hazard.

Dr. E. G. Heiselman, Fort Thomas, has been elected President of the Kentucky Obstetrical and Gynecological Society, and Dr. Douglas Haynes, Louisville, was elected Secretary and Treasurer.

Dr. Sam A. Overstreet, Louisville, was recently elected President of the staff of the Methodist Evangelical Hospital now under construction in Louisville. Others

Continued on page 60

now available

***DILAUDID**
Cough Syrup

for coughs that *must* be controlled

Formula: Each 5 cc. (1 teaspoonful) contains:
DILAUDID hydrochloride . 1 mg. (1/64 gr.)
Glyceryl guaiacolate . . 100 mg. (1½ gr.)
in a pleasant peach-flavored syrup containing 5 per cent alcohol.

Dose: 1 teaspoonful (5 cc.) repeated in three to four hours.
(for children adjust dose according to age)

*Subject to Federal narcotic regulations.

Dilaudid,® brand of dihydromorphinone, E. Bilhuber, Inc.

KNOLL PHARMACEUTICAL COMPANY
(formerly Bilhuber-Knoll Corp.)
ORANGE
NEW JERSEY

IN OFFICE SURGERY

ELECTIVE AND TRAUMATIC

use XYLOCAINE *first...*
as a local anesthetic
or a topical anesthetic

SWAB SPRAY INFILTRATION NERVE BLOCK

Xylocaine HCl solution, the versatile anesthetic for general office surgery, relieves pain promptly and effectively with adequate duration of anesthesia. It is safe and predictable. Local tissue reactions and systemic side effects are rare. Supplied in 20 cc. and 50 cc. vials; 0.5%, 1% and 2% without epinephrine and with epinephrine 1:100,000; also in 2 cc. ampules; 2% without epinephrine and with epinephrine 1:100,000.

XYLOCAINE® HCl SOLUTION
(brand of lidocaine*)

Astra Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.

SEE PDR

*U.S. PAT. NO. 2,441,498 MADE IN U.S.A.

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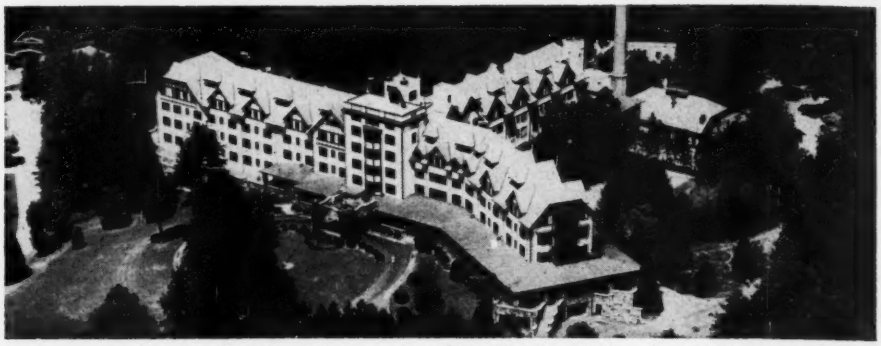

An Institution for the diagnosis and treatment of Psychiatric and Neurological illnesses, rest, convalescence, drug and alcohol habituation.

Insulin Coma, Insulin Sub-Shock, Electroshock and Psychotherapy are employed. The Institution is equipped with complete laboratory facilities including electroencephalography and X-ray.

Appalachian Hall is located in Asheville, North Carolina, a resort town, which justly claims an all around clime for health and comfort. There are ample facilities for classification of patients, rooms single or en suite.

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November 16-19, 1959

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INCREMIN® WITH IRON SYRUP

Lysine—Vitamins

BUILDS IRON RESERVES
BOOSTS APPETITE
PROMOTES GROWTH

Each daily teaspoonful dose (5 cc.) contains:	
l-Lysine HCl	300 mg.
Vitamin B_{12} Crystalline	25 mcgm.
Thiamine HCl (B_1)	10 mg.
Pyridoxine HCl (B_6)	5 mg.
Ferric Pyrophosphate (Soluble)	250 mg.
Iron (as Ferric Pyrophosphate)	30 mg.
Sorbitol	3.5 Gm.
Alcohol	0.75%

Bottles of 4 and 16 fl. oz.

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The **"OLD AGE SYNDROME"**

hasn't got him down!

NIATRIC™

For return to more normal, happier activity and improved behavior in the "Old Age Syndrome"—Niatric brings renewed interest and emotional relief from mild depression, confusion, and forgetfulness. Niatric improves circulation, helps to protect capillary integrity and to guard against the "little strokes" often found in your older patients suffering from symptoms of cerebral vascular insufficiency.

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SUNSHINE 360 DAYS OF THE YEAR!

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A MODERN HOSPITAL FOR EMOTIONAL READJUSTMENT

TARPON SPRINGS • FLORIDA ON THE GULF OF MEXICO

• Modern Treatment Facilities • Psychotherapy Emphasized • Large Trained Staff • Individual Attention • Capacity Limited • Occupational and Hobby Therapy • Supervised Sports • Religious Services Plus . . .

Your patients spend many hours daily in healthful outdoor recreation, reviving normal interests and stimulating better appetites and stronger bodies . . . all on Florida's Sunny West Coast.

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"Serpasil® has two special advantages in hypertension," say physicians in Syracuse

In Syracuse, as all over the world, physicians turn to Serpasil when its two special effects are needed for better management of hypertension:

1. The Central Effect: Serpasil calms patients who are frankly anxious or tense as well as hypertensive.

2. The Bradycrotic Effect: The heart-slowing effect of Serpasil relieves the tachycardia that so often accompanies high blood pressure.

These facts about Serpasil were found in reports from 450 physicians in the U. S. (part of a world-wide survey*): 74 per cent of *hyper-anxious hypertensives* treated with Serpasil showed excellent or good over-all response; 80 per cent of patients with *tachycardia* showed excellent or good response.

When marked anxiety-tension or tachycardia are part of the hypertensive picture, Serpasil can help your patient in more ways than one.

DOSAGE: Average initial daily dose, 0.5 mg. with a range of 0.1 to 1 mg. Reduce in one week to 0.25 mg. or less daily for maintenance.

SUPPLIED: *Tablets,* 0.1 mg., 0.25 mg., 1 mg., 2 mg. and 4 mg. *Elixirs,* 0.2 mg. and 1 mg. per 4-ml. teaspoon. *Samples available on request.*

*Complete information from this survey will be sent on request.

SERPASIL® (reserpine CIBA) 2/2632 MB

CIBA SUMMIT, NEW JERSEY

YOU'VE said good-by to the bride who was once your little girl, and to that handsome boy who is now your son. The youngsters are on their own: and so, after twenty-odd years, are you! Now is the time to think of yourselves—your pleasures, your security, your eventual retirement. A good time to start putting part of your savings away in safe, sure, United States Savings Bonds. Where nothing can touch your principal. And where your money earns 3¼% when bonds are held to maturity. Series E Bonds grow in value, year by year—and Series H Bonds pay you interest twice a year. Whichever you choose, start your bond program today! When financial independence counts, count on U. S. Savings Bonds!

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even when the causative organism may be a "persistent staph"

Cosa-Signemycin*

GLUCOSAMINE-POTENTIATED TETRACYCLINE WITH TRIACETYLOLEANDOMYCIN

increases the certainty of safe, rapid response

AS PROVED BY extensive clinical trials—an over-all success rate of more than 94% was achieved in a total of 3,280 cases.†

AS PROVED BY success in mixed infections—more than 95% of 1,000 acute and chronic respiratory tract infections were successfully treated; a 99% cure rate was achieved in mixed bacterial pneumonias.†

AS PROVED BY effectiveness in "problem infections"—a response rate better than 96% was recorded in a group of 221 gastrointestinal infections including chronic intestinal amebiasis; 91% of 465 urogenital infections were successfully controlled.†

AS PROVED BY excellent safety record—extremely well tolerated; discontinuance of medication was necessary in only 11 of 3,280 patients.†

A significant number of the above cases had not responded to other antibiotics.

Cosa-Signemycin is particularly valuable in home and office, where susceptibility testing is difficult or impractical.

SUPPLY: *Capsules* (green and white), 250 mg. and 125 mg.
New Oral Suspension (raspberry-flavored), 2 oz. bottle, 125 mg. per teaspoonful (5 cc.).
New Pediatric Drops (raspberry-flavored), 10cc. bottle, 5 mg. per drop, plastic calibrated dropper.

Average dosage: For adults, 1-2 Gm. daily in divided doses; proportionately less for children, depending on age, weight, and severity of infection.

†Literature and bibliography available on request.

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Pfizer *Science for the world's well-being* **PFIZER LABORATORIES,** *Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.*

CITY VIEW
SANITARIUM

For the diagnosis and treatment of nervous and mental disorders, and addiction to alcohol and drugs.

Established 1907

NASHVILLE, TENNESSEE

Continued from page 52

elected to the staff are: Dr. Henry Saam, Vice-President; Dr. M. M. Elliott, Secretary-Treasurer; Dr. J. B. Lukins, Chairman of the Department of Surgery; Dr. Woodford B. Troutman, Chairman of the Department of Medicine; Dr. J. D. Gordinier, Chairman of the Department of Obstetrics and Gynecology; and Dr. Eugene Kremer, Jr., Chairman of the Department of General Practice.

New officers of the Kentucky Physicians Mutual, Inc., include: Dr. J. Vernon Pace, Paducah, President; Dr. William J. Cartmell, Maysville, First Vice-President; and Dr. John Dickinson, Glasgow, Second Vice-President.

Dr. J. Murray Kinsman, Dean of the University of Louisville School of Medicine, has been elected Treasurer of the Association of American Medical Colleges. The Association sets standards for all American medical schools.

MARYLAND

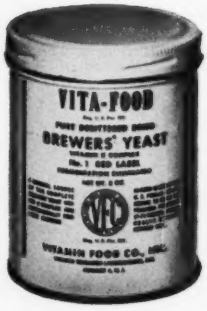
Dr. Christine W. Kehne, Director of the Psychiatric Youth Service, Montgomery County Health Department, is on leave of absence in order to serve a fellowship at Children's Hospital, awarded her by the National Institute of Mental Health.

MISSISSIPPI

New officers of the Mississippi Fellows of the Amer-

Continued on page 62

CLINICAL RESULTS . . .



in the therapy of many disorders have steadily improved as nutrition of the patient has been enhanced, with special attention to optimal levels of the *entire Vitamin B Complex* and *biologically complete Protein*—as in VITA-FOOD genuine Brewers' Yeast, which also supplies essential minerals, lipotropic and other factors; and is highly digestible even by severely depleted patients.

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RHINALL NOSE DROPS

For quick, effective relief of nasal congestion

Safe for both children and adults, Rhinall Nose Drops are pleasant to use, provide ventilation and drainage without irritation of the ciliated epithelium.

no burning or irritation • no risk of sensitization
no bad taste or after reactions

SUPPLIED: one-ounce dropper bottle: ½-ounce plastic spray bottle.

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Contains:
Phenylephrine Hydrochloride 0.15%
"Propadrine" Hydrochloride 0.3%
in an isotonic saline menstruum

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Continued from page 60

ican College of Surgeons are Drs. Archie C. Hewes, Gulfport, President; G. Swink Hicks, Natchez, President-Elect; and Jack V. King, Jackson, Secretary.

The Mississippi Society of Internal Medicine, an affiliate of the American Society of Internal Medicine, elected as officers Dr. A. Gayden Ward, Jackson, President, and Dr. John G. Archer, Greenville, Secretary.

MISSOURI

Dr. Preston C. Hall, St. Louis, has been chosen President-Elect of the Missouri Academy of General Practice. He is a Vice-President and a Past President of the St. Louis Academy of General Practice. Other new officers are Dr. William C. Allen, Glasgow, Vice-President, and Dr. John Pearl, St. Clair, Secretary-Treasurer.

Dr. Clarence M. Pickard, Columbia, and Dr. Earl Loyd, Jefferson City, have been appointed Clinical Associates in Medicine at the University of Missouri Medical Center.

Dr. Roscoe L. Pullen, Dean of the School of Medicine and Medical Director of the University Hospital, has just returned from San Juan, Puerto Rico, where he was invited to serve as a consultant in the planning of a new Medical Sciences Building for the University of Puerto Rico School at San Juan. Dr. Pullen has also been asked by the Arizona State officials to serve as a

Continued on page 64

TULANE UNIVERSITY
SCHOOL OF MEDICINE

Emergencies in Medicine	January 28-30, 1959
Pediatric Dermatology	February 16-21, 1959
Surgery of Trauma	February 26-28, 1959
Anesthesia	March 5- 7, 1959
Pediatric Hematology	April 9-11, 1959

Postgraduate Medical Trainee Program

This program, available in most of the clinical departments, is a means of offering postgraduate training adapted to the interests and needs of individual physicians. Letters of application describing the duration (one week to one year) and type of program desired are reviewed with the department concerned and accepted whenever possible.

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treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM

. . . in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

Write for samples.

FOSTEX CAKE

. . . in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

WESTWOOD PHARMACEUTICALS Buffalo 13, New York

Continued from page 62

consultant in the building of a new medical school there.

It has been announced that the American Diabetes Association has appointed Dr. Henry E. Oppenheimer, St. Louis, as governor of Missouri for a three year term.

Dr. Louis T. Byars, St. Louis, has been installed as President of the American Society of Plastic and Reconstructive Surgery at a recent meeting of the society.

Dr. James B. Brown, St. Louis, Professor of Surgery at Washington University School of Medicine, has been elected Second Vice-President of the American College of Surgeons.

Dr. Bert H. Klein, St. Louis, is the new President of the medical staff of Deaconess Hospital, succeeding Dr. Birkle Eck, St. Louis. Dr. Guerdan Hardy, Clayton, was elected Vice-President, and Dr. Lee A. Hall, St. Louis, Secretary.

Officers of the Missouri Society of Anesthesiologists for 1958-59 are President, Dr. Edward O. Kraft, Brentwood; President-Elect, Dr. Leon H. Rubnitz, Kansas City; Vice-President, Dr. Kenneth K. Keown, Columbia; and Dr. Harry C. Sammons, Kirkwood, Secretary-Treasurer.

Dr. E. Lee Dorsett, Assistant Professor of Obstetrics and Gynecology at St. Louis University, spent several weeks in Port-au-Prince, Haiti, in December where he delivered a number of lectures at the Medical College of Haiti.

NORTH CAROLINA

Dr. David R. Hawkins, Associate Professor of Psychiatry, University of North Carolina School of Medicine, Chapel Hill, has been appointed a member of the Mental Health Small Grant Committee of the National Institute of Mental Health for a term of four years.

Dr. Herbert A. Saltzman, who is now on the faculty of Duke University School of Medicine, Durham, has been awarded the Air Force Commendation Medal by direction of the Secretary of the Air Force.

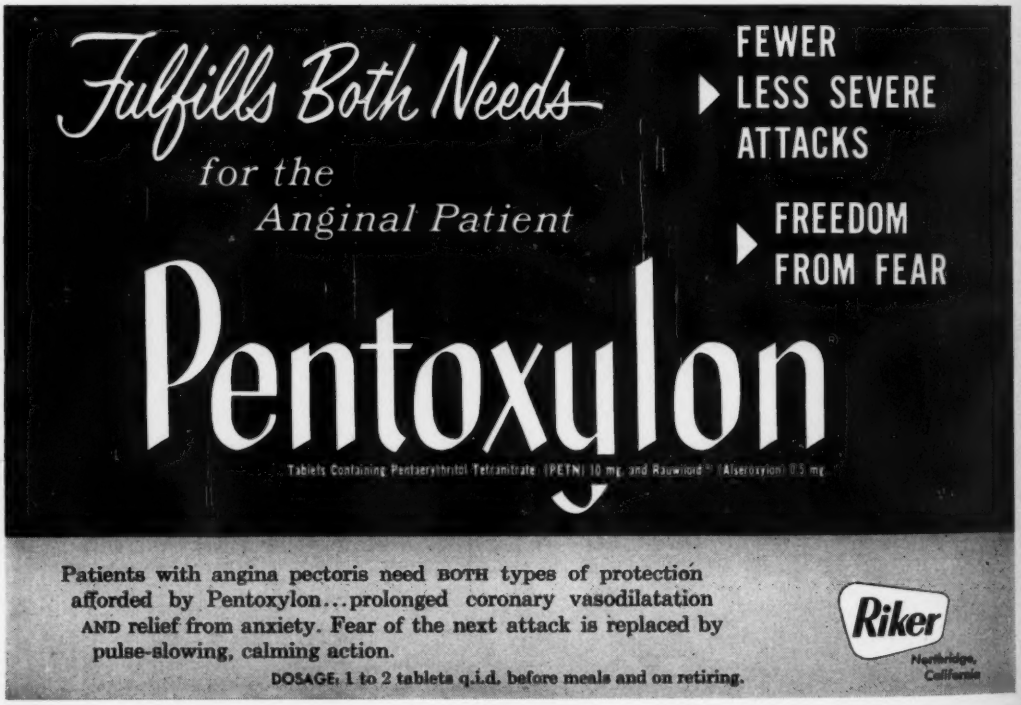
At its November meeting held in Sea Island, Georgia, the North Carolina Surgical Association elected as officers Dr. John A. Brabson, Charlotte, President; Dr. Isaac E. Harris, Jr., Durham, President-Elect; Dr. Theodore S. Raiford, Asheville, Vice-President; and Dr. Alfred Hamilton, Raleigh, Secretary-Treasurer.

The private medical library of the late Dr. J. C. Pass Fearrington of Winston-Salem has been donated to the University of North Carolina Division of Health Affairs Library. The collection of books and journals numbers some 3,000 volumes and is valued at an estimated $28,000. The Division of Health Affairs Library serves the UNC Schools of Dentistry, Medicine, Nursing, Pharmacy, Public Health, and N. C. Memorial Hospital.

OKLAHOMA

Dr. George H. Garrison, Oklahoma City pediatrician, has been appointed by the American Medical As-

Continued on page 66


Fulfills Both Needs
for the
Anginal Patient
FEWER
LESS SEVERE
ATTACKS
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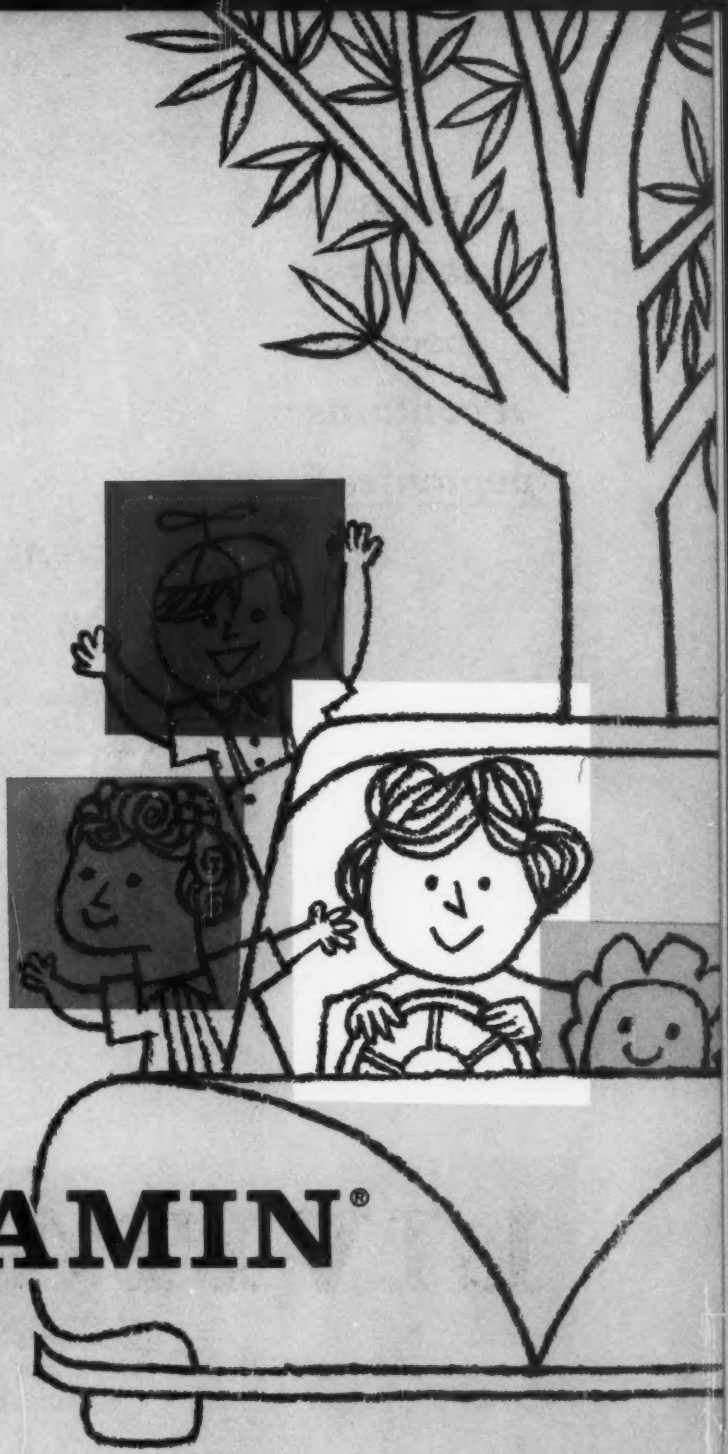
FROM FEAR
Pentoxylon
Tablets Containing Pentaerythritol Tetranitrate (PETN) 10 mg. and Rauwiloid® (Alseroxylon) 0.5 mg.
Patients with angina pectoris need BOTH types of protection afforded by Pentoxylon...prolonged coronary vasodilatation AND relief from anxiety. Fear of the next attack is replaced by pulse-slowing, calming action.
DOSAGE: 1 to 2 tablets q.i.d. before meals and on retiring.
Riker
Northridge, California

During her reproductive years— almost every woman needs iron therapy



The average woman loses 1 mg. of iron per day through normal elimination. Add to this an average of 15 to 30 mg. each menstrual period.[1] It is evident that many women deplete their iron reserves faster than the normal diet can replenish them.

Many clinicians recommend that every woman, during her reproductive years, receive iron therapy for six weeks each year.

Livitamin, with *peptonized* iron, offers an excellent formula to restore depleted iron reserves. Peptonized iron is well absorbed and stored, and less irritating than other forms. The Livitamin formula, which contains the B complex, provides integrated therapy to normalize the blood picture.

1. Brown, E.B., Jr. *The Management of Iron Deficiency Anemia*, GP, 2:87 (Feb. 1958).

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FORMULA: Each fluidounce contains:

Iron peptonized (Equiv. in elemental iron to 71 mg.)	420 mg.
Manganese citrate, soluble	158 mg.
Thiamine hydrochloride	10 mg.
Riboflavin	10 mg.
Vitamin B_{12} Activity (derived from Cobalamin conc.)	20 mcg.
Nicotinamide	50 mg.
Pyridoxine hydrochloride	1 mg.
Pantothenic acid	5 mg.
Liver fraction 1	2 Gm.
Rice bran extract	1 Gm.
Inositol	30 mg.
Choline	60 mg.

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current studies show peptonized iron*

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*Keith, J.H.: Utilization and Toxicity of Peptonized Iron and Ferrous Sulfate, Am. J. Clin. Nutrition *1*:35 (Jan.-Feb., 1957).

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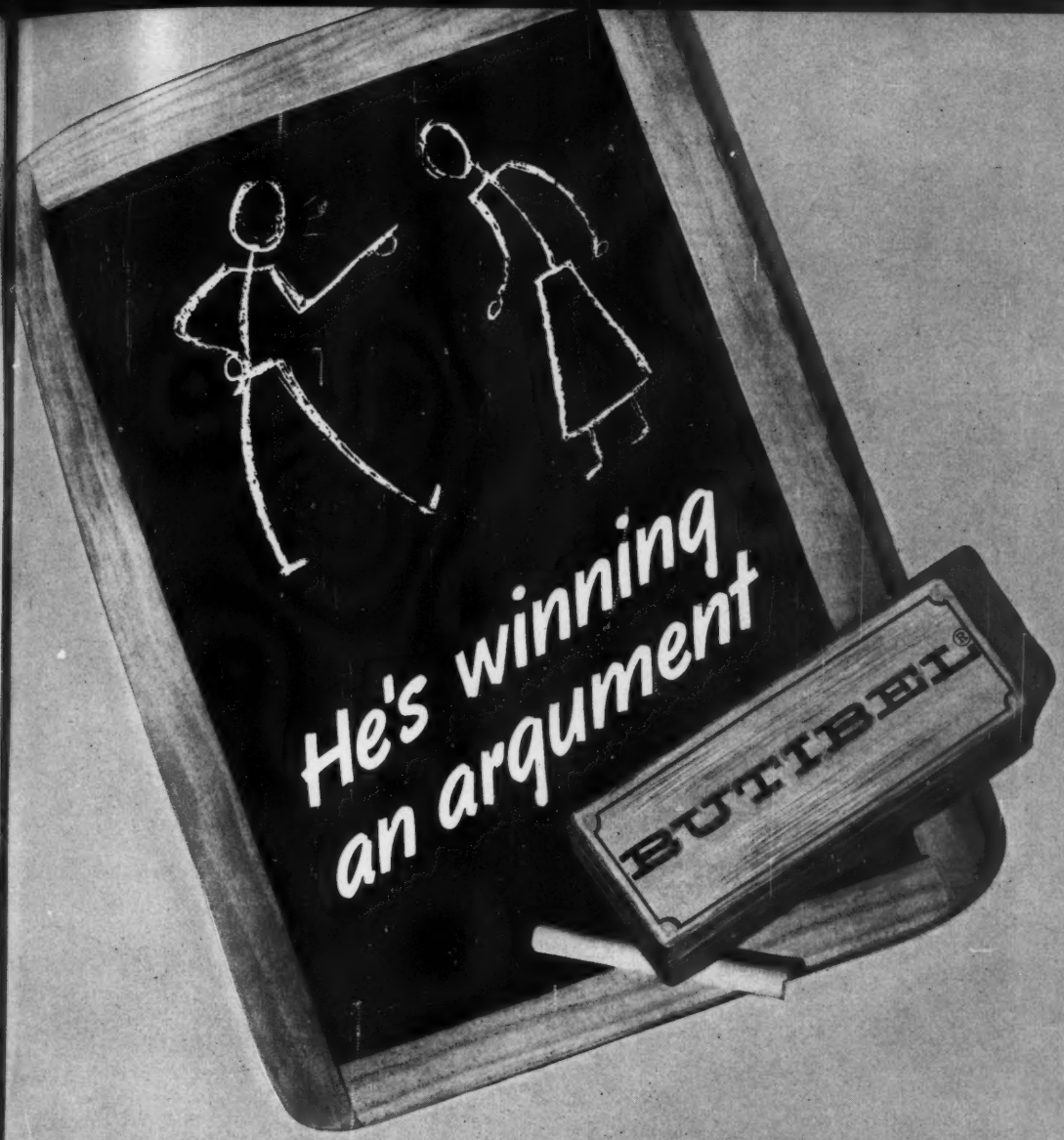

but his stomach and nerves are losing to the "jitters" of spasm and irritability.

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natural belladonna, 15 mg.—more effective than the synthetic alkaloids.
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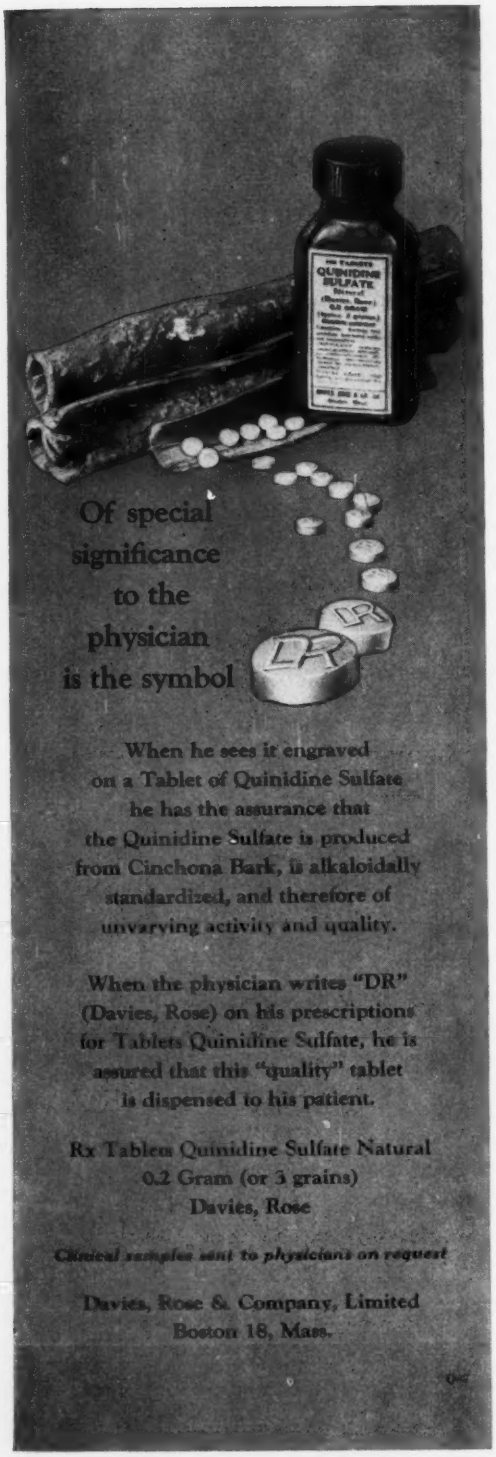
1. Maynert, E. W. and Losin, L.: J. Pharmacol. & Exper. Therap. *115*:275-282 (Nov.) 1955.
2. Butler, T. C. et al.: J. Pharmacol. & Exper. Therap. *111*: 425 (Aug.) 1954.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When he sees it engraved on a Tablet of Quinidine Sulfate he has the assurance that the Quinidine Sulfate is produced from Cinchona Bark, is alkaloidally standardized, and therefore of unvarying activity and quality.
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Rx Tablets Quinidine Sulfate Natural
0.2 Gram (or 3 grains)
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Davies, Rose & Company, Limited
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Continued from page 64

sociation to serve on the Community Health Advisory Committee of the United States Junior Chamber of Commerce.

Dr. Louis H. Ritzhaupt, Guthrie, will become the new Dean of the Oklahoma Senate when the Legislature convenes for its 27th session this month.

Dr. Alfred T. Baker, President-Elect of the Oklahoma State Medical Association, Durant, has been elected to the Board of Directors of the Oklahoma Society of Crippled Children.

Dr. Ralph Heine, Elk City, was one of seven physicians in the nation to be approved for membership in the American Fracture Association during the group's recent convention in Oklahoma City.

Ten Oklahoma physicians were inducted as new Fellows of the American College of Surgeons which met recently. They are: Dr. William S. Dandridge, Muskogee; Dr. Gilbert S. Campbell, Dr. Merlin K. DuVal, Jr., Dr. Edward R. Munnell, Dr. Bob J. Rutledge, of Oklahoma City; Dr. Robert L. Imler, Jr., Dr. Emanuel N. Lubin, Dr. Joe L. Spann, Dr. Byron W. Steele, Jr., and Dr. C. Thomas Thompson, of Tulsa.

SOUTH CAROLINA

Dr. C. Guy Castles, Columbia, took over as President of the South Carolina Pediatric Society at its annual meeting, succeeding Dr. Fred Adams, Spartanburg. Dr. C. H. Zemp, Camden, became Vice-President, and Dr. Kenneth Herbert, Charleston, became Secretary-Treasurer.

Appointment of Dr. H. W. Herbert, Charlottesville, as Clinical Director of the Darlington-Florence Mental Health Clinic was announced by Dr. W. P. Beckman, State Director of Mental Health.

Dr. F. Raymond Price, Charleston, has been elected President of the South Carolina Ophthalmology and Otolaryngology Society. Other officers elected were: Dr. Robert E. Livingston, Newberry, Vice-President; Dr. Roderick MacDonald, Rock Hill, Secretary-Treasurer; and Dr. L. D. Lide, Florence, President-Elect.

TENNESSEE

Dr. Franklin B. Bogart, Chattanooga, has been named First Vice-President of the American Roentgen Society, at its recent meeting in Washington, D. C.

The new officers of the Memphis Society of Pathologists are Dr. George Lumb, President; Dr. Robert Gourley, Vice-President; Dr. Richard Walker, Secretary-Treasurer; and Dr. Scott Gilmer, Immediate Past President.

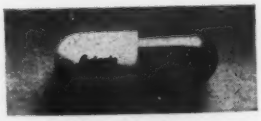
Drs. Mark P. Fecher and William K. Rogers, Knoxville, Drs. Gilbert A. Rannick and Howell Sherrod, Johnson City, have been named Fellows of the American College of Surgeons.

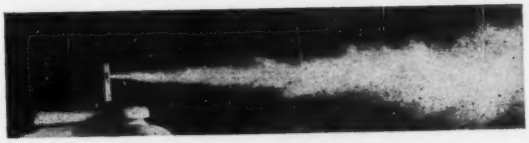
Dr. Richard C. Sexton, Knoxville, has assumed Presidency of the East Tennessee Heart Association. President-Elect of the organization is Dr. John W. Avera, Knoxville.

The following nine Memphis physicians have been

Continued on page 70

in a form to fit

every antibiotic 

need  ...

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Rauwiloid

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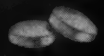
Rauwiloid provides effective Rauwolfia action virtually free from side effects... the smooth therapeutic efficacy of Rauwiloid is associated with significantly less toxicity than reserpine... and with a lower incidence of depression. Tolerance does not develop.

Rauwiloid is initial therapy for every hypertensive patient. ...Dosage adjustment is never a problem...



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Although *continuous* ultrasound therapy is widely used throughout the country, *pulsed* energy is a relatively new development. Its advocates claim greater clinical effectiveness because the mechanical action can be increased with far less accumulation of heat. When the UT-400 is used for pulsed ultrasound, there is a duty factor of 20%.

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Continued from page 66

named Fellows of the American College of Surgeons: Drs. Anthony P. Jerome, Joseph H. Brock, Robert S. Caradine, Jr., Lawrence H. Cohen, Wade H. Etheridge, George R. Livermore, Jr., John J. McCaughan, Jr., William L. Northern, Jr., and Earle L. Wrenn, Jr.

Dr. W. A. Jackson, Morristown, is the new Health Director of the Hamblen-Jefferson-Cocke Counties health districts.

Dr. E. Kent Carter, Kingsport, has been named President of the East Tennessee Radiological Society.

Dr. Ben Hall, Johnson City, has been named President-Elect of the Tennessee Heart Association.

The formation of a Medical Group in Nashville, The Miller Clinic, has been announced with the following personnel: General Surgery, Drs. Cleo M. Miller, R. Glenn Hammonds, and Jackson Harris; Orthopedic Surgery, Dr. Arthur L. Brooks; Internal Medicine, Drs. Russell D. Ward, Clarence C. Woodcock, Jr., James M. Hudgins, and Joseph D. Robertson; Pediatrics, Drs. Dewey G. Nemec and P. C. Elliott; Radiology, Dr. M. Dee Ingram, Jr.

TEXAS

The Temple Division of the University of Texas

Continued on page 74

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REFERENCES: 1. Miller, J. H., et al.: Am. J. Dig. Dis. 3:229-231, 1958.
2. Swartzwelder, J. C., et al.: A.M.A. Arch. Int. Med. 101:658-61, 1958.
3. Frye, W. W., et al.: Am. J. Trop. Med. Hyg. 6:890-93, 1957.
4. Swartzwelder, J. C., et al.: J.A.M.A. 165:2063-67, 1957.

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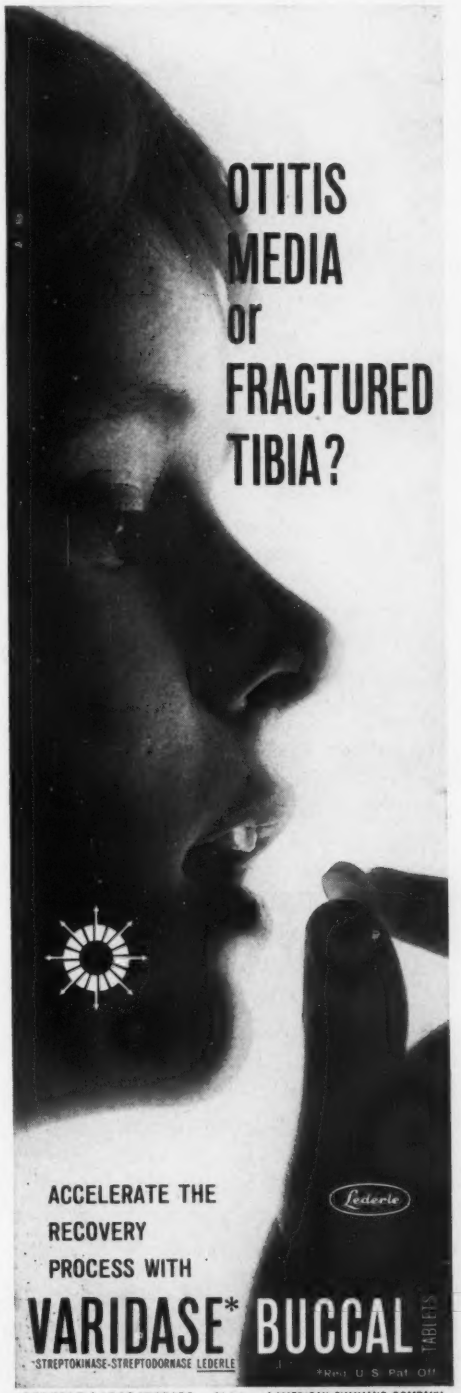

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B. Marden Black, M.D. .....*Rochester, Minn.*
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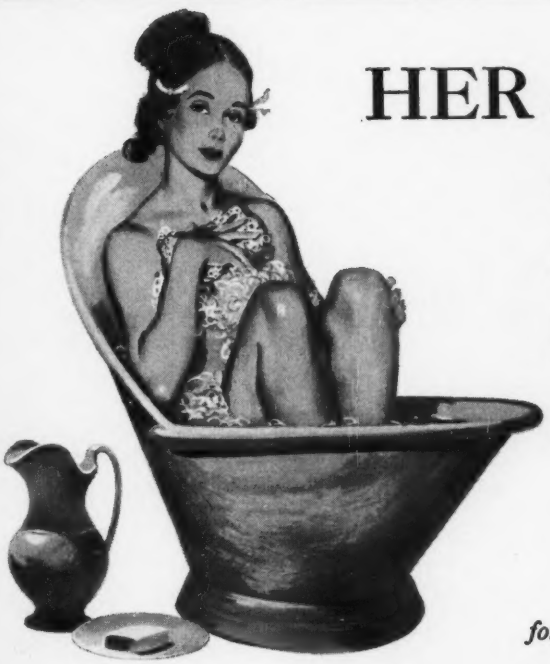

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Continued from page 70

Postgraduate School of Medicine announces its Seventh Postgraduate Conference stressing "Current Topics in Medicine and Surgery." This program, sponsored by Scott, Sherwood and Brindley Foundation, will be presented in Temple on March 2, 3, 4, 1959. Registration forms are available from the office of the Assistant Dean, University of Texas Postgraduate School of Medicine, Temple Division, Temple, Texas.

Dr. William P. Wilson, Assistant Professor of Psychiatry and Neurology, Duke University, Durham, North Carolina, has been appointed Director of Psychiatric Research and Professor of Psychiatry and Neurology, University of Texas Medical Branch, Galveston.

Dr. D. Bailey Calvin, formerly Dean of Students and Curricular Affairs, University of Texas Medical Branch, Galveston, has been made Director of the Office of Research Grants and Contracts.

VIRGINIA

The new President of the Medical Society of Virginia is Dr. Walter P. Adams, Norfolk. The President-Elect is Dr. Allen Barker, Roanoke; First Vice-President, Dr. Guy W. Horsley, Richmond; Second Vice-President, Dr. James Peery, Cedar Bluff; and Third Vice-President, Dr. McLemore Birdsong, Charlottesville.

New officers of the Southwest Virginia Medical Society, are Dr. J. G. Cox, Hillsville, President; Dr. W.

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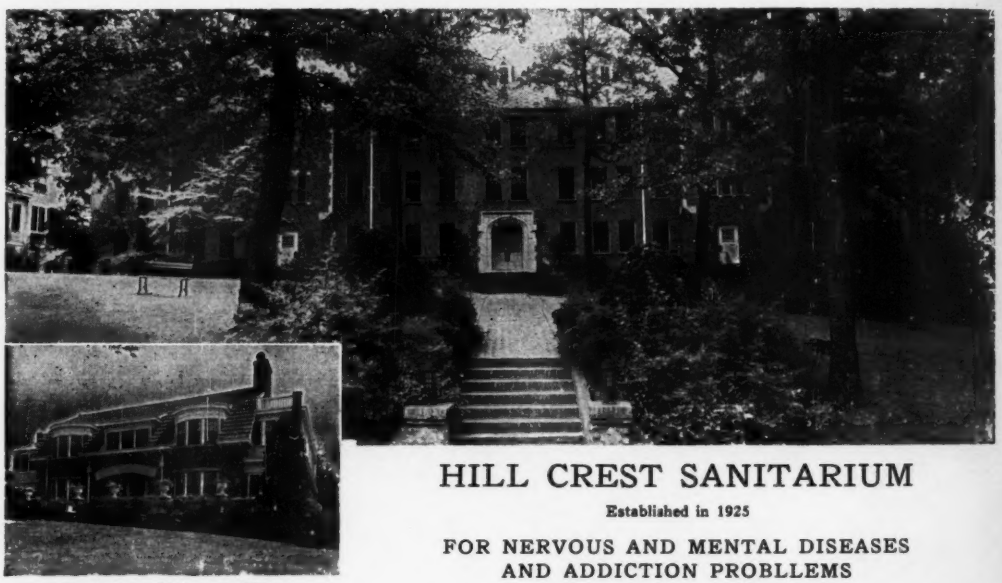

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Continued from page 74

S. Credle, Bristol, Vice-President; and Dr. M. A. Johnson, Roanoke, Secretary-Treasurer.

Dr. A. Warner Lewis, Sr., Aylett, was recently honored by the King William Ruritan Club for his "long and faithful service" to the rural people of this and adjoining counties.

Dr. Byrd S. Leavell, Charlottesville, has been named Assistant Dean of the University of Virginia School of Medicine. He will succeed Dr. Henry B. Mulholland who has retired from this position.

Dr. Benedict Nagler, Superintendent of the Lynchburg Training School and Hospital, has been invited by the Director of the National Institute of Health, Bethesda, Maryland, to become a member of the Neurology Field Investigations Committee of the National Institute of Neurological Diseases and Blindness.

Dr. Samuel H. Carter, Verona, has been named as the physician for Mary Baldwin College, Staunton, succeeding Dr. Paxton Powers.

Dr. Weir M. Tucker, Richmond, has been appointed as Chairman of the newly created Division of Neurology of the Medical College of Virginia.

Dr. Houston L. Bell has been elected President of the Roanoke Unit of the American Cancer Society.

Dr. William D. Dolan has been elected President of the Arlington Unit of the American Cancer Society.

Dr. Richard H. Cross, Concord, has been presented the Concord Ruritan Citizenship Award as the community's outstanding citizen of 1958.

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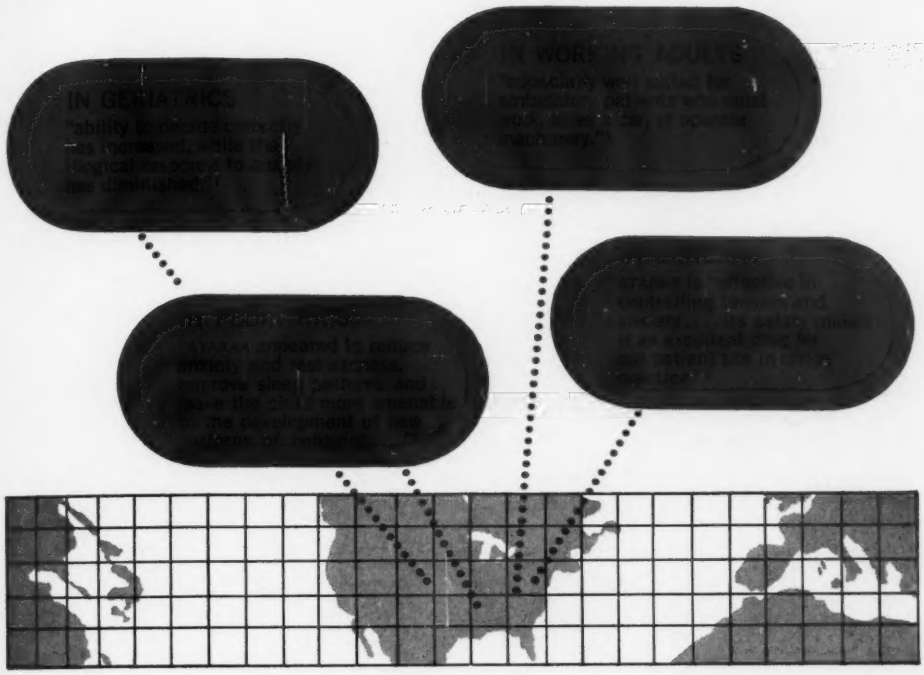

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References: 1. Smigel, J. O., et al.: J. Am. Ger. Soc., in press. 2. Freedman, A. M.: Pediat. Clin. North America 5:573 (Aug.) 1958. 3. Ayd, F. J., Jr.: New York J. Med. 57:1742 (May 15) 1957. 4. Menger, H. C.: New York J. Med. 58:1684 (May 15) 1958. 5. Coirault, M., et al.: Presse méd. 64:2239 (Dec. 26) 1956. 6. Bayart, J.: Presented at the International Congress of Pediatrics, Copenhagen, Denmark, July 22-27, 1956.

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(1) Estimate based on epidemiologic study by Van Volkenburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122, Jan. 1933.
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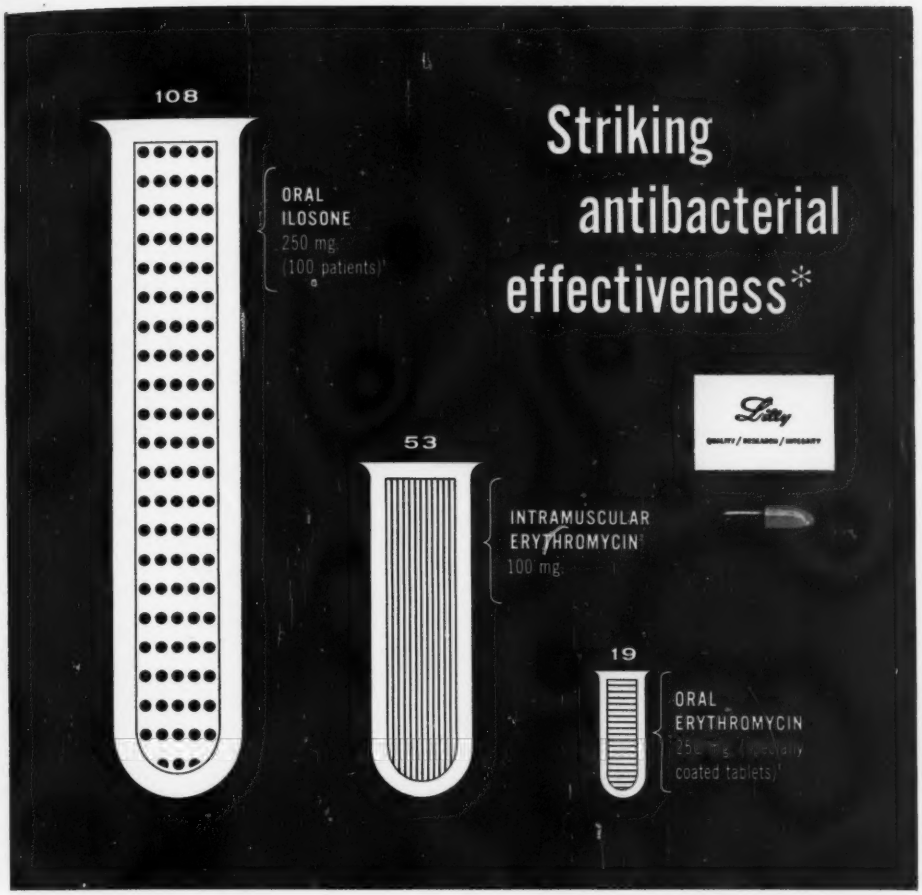

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1. Griffith, R. S., *et al.*: Antibiotic Med. & Clin. Therapy, *5*:609 (October), 1958. Note: Peak levels with the oral erythromycin tablets (thirty-three dilutions) were not observed until four hours after administration. 2. Data from Griffith, R. S.: Antibiotics Annual, p. 269, 1954-1955.

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